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THE CLASSIFICATION OF TUMORS OF THE THYROID*

By SHIELDS WARREN, M.D.

From the New England Deaconess, New England Baptist and Collis P. Huntington Hospitals
BOSTON, MASSACHUSETTS

IN THE classification of thyroid tumors there is an opportunity for the correlation of certain types of clinical behavior with certain morphologic entities. Classification on the basis of etiology is completely unsatisfactory because the origin of no type of thyroid tumor is known. Fortunately, morphologic characteristics and clinical behavior tend to parallel one another in certain groups of thyroid tumors[1,2,3]

Classification of Thyroid Tumors

Benign:
1. Adenoma
   a. embryonal
   b. fetal
   c. simple
      1. Hürthle cell
   d. colloid
2. Papillary cystadenoma
   a. originating from thyroid
   b. originating from aberrant thyroid

Malignant:

Group I. Low or Potential Malignancy
1. Adenoma with blood vessel invasion
2. Papillary cystadenoma with blood vessel invasion
   a. originating from thyroid
   b. originating from aberrant thyroid

Group II. Moderate Malignancy
1. Papillary adenocarcinoma
2. Alveolar adenocarcinoma
3. Hürthle cell adenocarcinoma

Group III. High Malignancy
1. Small cell carcinoma (carcinoma simplex)
   a. compact type
   b. diffuse type
2. Giant cell carcinoma
3. Epidermoid carcinoma
4. Fibrosarcoma
5. Lymphoma

In the adenomas of the thyroid there is but little chance for confusion. All of these tumors are benign in their clinical behavior. All are encapsulated. All compress the adjacent thyroid tissue. All present a histologic picture uniform for each type throughout their substance. The only source of confusion is their differentiation clinically and in gross from the nodules of endemic goiter which may sometimes simulate them very closely. The true adenomas are neoplasms. The nodules in endemic goiter are foci of either excess colloid storage or of compensatory formation of new follicles.

The adenomas can be divided according to their degree of differentiation, ranging from the least differentiated to the most: first, the embryonal in which there is no or very little evidence of follicle formation; then, the fetal in which numerous, rather poorly formed follicles are present; the simple in which well-developed follicles occur; and the colloid in which all the follicles

* Read at the Forty-first Annual Meeting, American Roentgen Ray Society, Boston, Mass., Oct. 1–4, 1940.

Fig. 1. Adenoma of thyroid. Note definite encapsulation and compressed normal thyroid substance.

present are widely distended with secretion. One rare form is the Hürthle cell type, in which the cells are large, clear, and acidophilic. The adenomas when removed usually weigh from 25 to 200 gm. and rarely exceed 10 cm. in diameter.

These adenomas are not dangerous in themselves. They are a problem chiefly from the standpoint of the possible development of malignancy in them. The statement has been made, although difficult to prove, that 80 per cent of thyroid cancers arise in pre-existing adenomas. An isolated nodule in the thyroid has about ten times greater chance of being a malignant tumor than any other type of thyroid enlargement. Very rarely adenomas may be multiple.

The papillary cystadenoma may arise from the thyroid proper or from lateral aberrant thyroid tissue. This tumor may be single, but is often multiple. The nodules are well encapsulated, rather soft, and rarely exceed 5 cm. in diameter. On microscopic study, they are seen to consist of irregular papillary projections, coated by a single layer of columnar epithelium. Here and there are a few thyroid follicles with apparently normal colloid. So long as these tumors do not show vascular or capsular invasion they are benign.

When we subdivide the malignant tumors of the thyroid on the basis of their histologic aspect, we find that they fall rather naturally into three clinical groups: those of low or potential malignancy, including the adenomas with blood vessel invasion, the proliferating struma of Langhans, as well as the papillary cystadenoma with blood vessel invasion. These tumors are well differentiated and distinguishable from their benign, closely related forms only by evidence of intravascular growth. We have excluded certain of the cases utilized in our 1935 study as we feel we have been able to delimit more clearly our criteria for blood

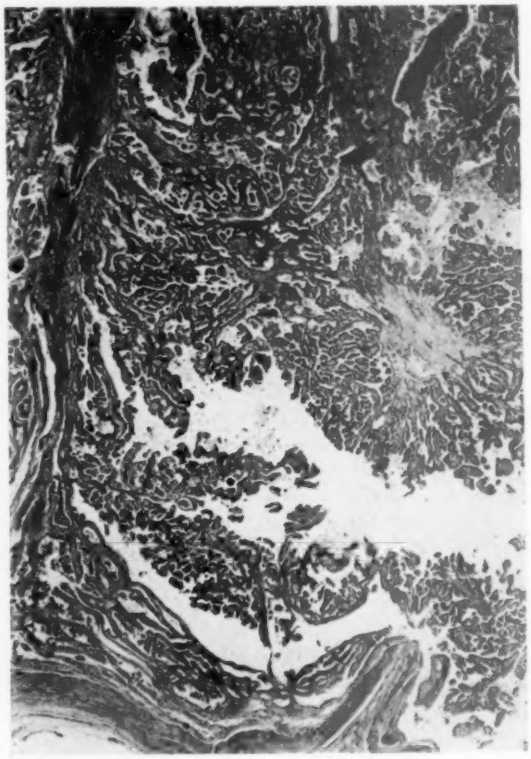

Fig. 2. Papillary cystadenoma (benign). ×12.5

vessel invasion. These tumors, while potentially malignant from the pathologic standpoint, must be considered cancer clinically as they may kill by local growth or metastasis.

The somewhat less differentiated tumors make up the second group, that of the tumors of moderate malignancy. These include the adenocarcinomas which may be either papillary, alveolar or very rarely of the Hürthle cell type. The distinction between these types has to be made on microscopic grounds, the papillary showing often several layers of actively proliferating epithelium over papillary projections, the alveolar showing various degrees of follicle formation but without papillary projections, and the Hürthle cell made up of large, clear, acidophilic cells usually in alveolar arrangement. The distinction between the papillary and the alveolar type is usually worth while to make as response to irradiation is much more satisfactory in the former than in the latter in Dr. Hare's experience.

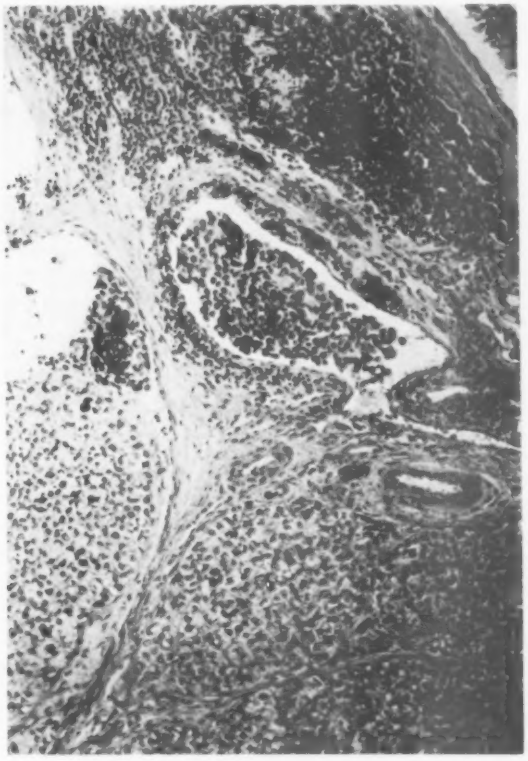

Fig. 3. Papillary adenocarcinoma of the thyroid showing invasion of blood vessel. ×150

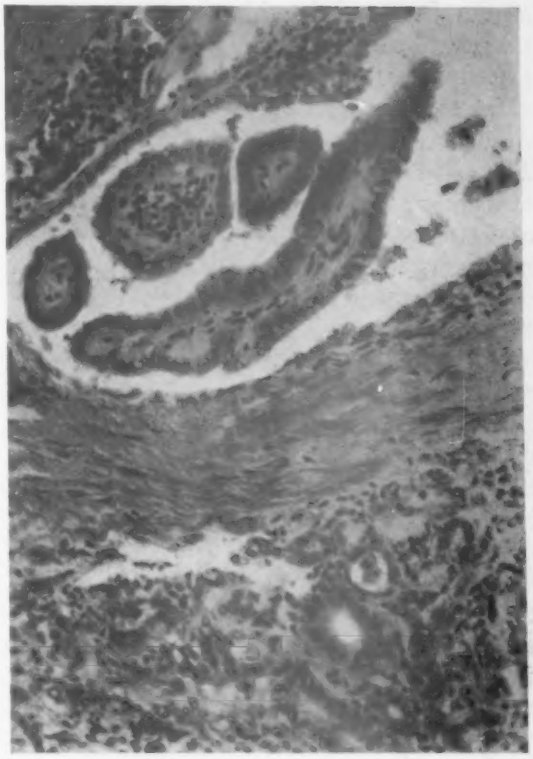

Fig. 4. Small cell carcinoma (carcinoma simplex), compact type. Note blood vessel invasion. ×100

In the third group are placed the tumors of high malignancy. These are anaplastic and, with the exception of the giant cell carcinoma, are responsive to irradiation. Carcinoma simplex or small cell carcinoma is the most frequent and fortunately most radioresponsive of these. This occurs in two forms: that in which the cells are closely massed together, the compact type; that in which they are spread irregularly through the tissue, the diffuse type. This diffuse type may readily be mistaken for a lymphomatous involvement of the gland on histologic examination. Perhaps the most distinctive of this group of highly malignant thyroid tumors is the giant cell carcinoma, frequently spoken of as carcinosarcoma. This tumor, which we believe to be epithelial in origin, usually occurs in elderly people who give a history of a

nodule in the neck which had persisted for some time and then suddenly began to grow rapidly. These tumors are highly vascular, extremely rapidly growing, and extend widely through the tissues of the neck. They usually kill the patient with local involvement before any very marked degree of metastasis has occurred. Extremely rarely among the group of highly malignant tumors occurs the epidermoid carcinoma which may originate either from thyroglossal duct epithelium or from metaplasia of the thyroid epithelium proper. The epidermoid carcinoma of thyroglossal duct origin may occur in very young people. I have seen one fatal case in a nine-year-old boy. True fibrosarcoma of the thyroid is a very rare tumor. It resembles histologically and grossly fibrosarcoma elsewhere and like that occurring in other tissues is resistant to irradiation. Some of the reported instances of fibrosarcoma are apparently cases of giant cell carcinoma. Finally, there may occur in extremely rare instances, true lymphomas of the thyroid gland, presumably originating from the lymphoid infiltration which may occur in the thyroid either with advancing years or with various inflammatory or irritative states. This, of course, has a high degree of radiosensitivity, but an extremely low degree of radiocurability.

It is important for a clear-cut evaluation of clinical results of therapy of tumors of the thyroid that there be as uniform as possible a classification of these tumors. When, for example, some consider practically all of the papillary tumors benign and others divide them between the benign and malignant group on the basis of the generally accepted criteria of malignancy, there will obviously be a considerable discrepancy in the results of therapy.

This classification is proposed not as a final one, but as a fairly simple way of readily distinguishing new growths that will enable those using it not only to pigeonhole their tumors with some degree of ease and accuracy, but in addition to compare and appraise their therapeutic results with those of others.*

REFERENCES

1. Clute, H. M., and Warren, S. Cancer of the thyroid gland. *Am. J. Cancer*, 1931, *15*, 2563–2582.
2. Haagensen, C. D. Cancer of the thyroid; its radiosensitivity. *Am. J. Cancer*, 1931, *15*, 2063–2105.
3. Clute, H. M., and Warren, S. Prognosis of thyroid cancer. *Surg., Gynec. & Obst.*, 1935, *60*, 861–874.

* For discussion see page 473.

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RADIATION TREATMENT OF CARCINOMA OF THE THYROID*

By HUGH F. HARE, M.D.
Department of Radiology, The Lahey Clinic
BOSTON, MASSACHUSETTS

SUCCESSFUL results of the radiation treatment of malignant disease of the thyroid gland have been noted over a period of the past forty years. An attempt to correlate the various types of carcinoma of the thyroid with the method and the amount of treatment necessary to bring about permanent good results has been the goal of radiologists during this interval.

Seven hundred and twenty-five persons die annually of thyroid cancer. This represents two-thirds of 1 per cent of all malignant disease in the United States registration area. Of these deaths, 44 per cent might be prevented by a combination of surgery and radiation treatment.

The average age of individuals with thyroid cancer is forty-eight years. Forty per cent have been under forty-five years of age, indicating that the disease is prevalent in the younger age group. The ratio of females to males is five to one.

The clinical grouping of thyroid cancers has corresponded well with the pathologic grouping. As has been previously stated, it also represents a method by which prognosis may be given and a background for comparison of results may be obtained.

In Group I are the patients with low grade or potential malignancy pathologically. Clinically, these are slowly growing tumors which may recur locally in lymph nodes, in mediastinal glands or may metastasize to bone by way of the blood stream. They have in the past been known as the "benign metastasizing goiters." It is impossible to differentiate adenoma with blood vessel invasion from papillary cystadenoma with blood vessel invasion clinically. These tumors are known to be radioresponsive, that is, the tumor will decrease in size or disappear except for residual scarring. The tumor dose is 4,800 r or less when the radiation is given by the protracted method. In several instances inoperable tumors have been made operable while others which were recurrent have been kept inactive over a period of five to seven years.

Case 1 represents a Group I type of tumor.

CASE 1. A woman, aged fifty-two, entered the Clinic in September, 1928, giving a history of goiter of three years' duration. Thyroidectomy was performed. The pathological report was embryonal adenoma with blood vessel invasion, malignant. Moderate doses of roentgen rays were given.

The patient was symptom-free until June, 1934, when she returned. There was a nodule, 1 cm. in diameter, in the skin of the neck on the right side, above the thyroidectomy scar. The pathological report following excision showed it to be aberrant thyroid tissue, with moderate hyperplasia.

The patient returned one year later, in June, 1935, with a multiple chain of nodes in the right side of the neck, and with extensive invasion of muscle. Biopsy alone was done which showed aberrant thyroid tissue with hyperplasia.

In January, 1940, the patient returned complaining of headaches and of a mass in the left side of the skull. Roentgenograms revealed a destructive lesion in the left parietal region consistent with metastatic disease. The mass was removed and pathological studies demonstrated embryonal adenoma with blood vessel invasion, malignant. The tumor presented the same characteristics microscopically as those noted in September, 1928.

In Group II are the patients with more rapidly growing malignant disease. These tumors are divided into two pathological types: papillary adenocarcinoma and alveo-

* Read at the Forty-first Annual Meeting, American Roentgen Ray Society, Boston, Mass., Oct. 1–4, 1940.

lar adenocarcinoma. In this instance the clinical classification does not follow the pathological classification as evidenced by differences in the percentages of five year survivals. The papillary adenocarcinomas with which there was an 80 per cent five year survival were much more amenable to treatment than the alveolar type with 27 per cent five year survivals. Recurrences may be local or widespread.

Papillary adenocarcinomas are radioresponsive and radiocurable; the alveolar types are resistant to irradiation in most instances, as has been shown by the small percentage of five year survivals. In one instance 6,000 r was given through one portal to a patient whose tumor was inoperable. The tumor became smaller and operable, but at operation it retained the same characteristics as found in the biopsy specimen prior to the heavy irradiation. It is in the alveolar adenocarcinomas that further attempts must be made to give enough radiation eventually to destroy the tumor.

Case II. A man, aged forty-five, entered the Clinic in October, 1934, with a history of goiter of six years' duration. Recently he had noted rapid increase in the size of the goiter. The tumor was partially excised; the pathological report was alveolar adenocarcinoma. A portion of the tumor was substernal and for this reason radon gold seeds were placed beneath the sternum and behind the left sternoclavicular joint, to give a total dose of 2,000 millicurie-hours of radon in gold seeds. The radon application was followed three weeks later by protracted irradiation, for a total dose of 4,800 r.

Radiation dermatitis was marked following this, but the skin eventually healed. At last examination six weeks ago the patient appeared to be healthy and there was no evidence of recurrence of malignancy.

In Group III are placed the relatively anaplastic tumors, those which are rapidly growing and those in which the average life duration is less than one year. These tumors invade locally, are widespread and frequently metastasize to the lungs.

Tumors of Group III, with the exception of the giant cell tumor which in all instances has been resistant to irradiation, are radioresponsive and with the dosage of roentgen rays employed, become clinically inactive in the region treated when 4,800 r has been delivered to the tumor bed.

Case III. A girl, aged nine, entered the Clinic November 26, 1934, with a history of enlargement of the neck of two months' duration. Operation was performed and the tumor was found to be carcinoma simplex, small cell compact type, with blood vessel invasion, lateral aberrant thyroid, with metastases to the lymph nodes. Radiation treatment by the divided dose method was given between December 6, 1934, and January 12, 1935, a total dose of 4,800 r being delivered to the skin. Roentgen treatment was discontinued due to severe radiation sickness which required hospitalization. A remaining nodule in the right side of the neck required radon application, in February 1935, at which time 400 millicurie-hours of radon was placed in the residual nodule.

The patient has remained well to date. There has been no evidence of a recurrence of the tumor. The blood cholesterol on December 9, 1936, was 153 mg., and on June 15, 1938, 130 mg., indicating normal thyroid activity.

Radiation Treatment. Radiation treatment was given postoperatively in all cases following as complete surgical removal as possible and after a careful, pathologic diagnosis had been made by Dr. Shields Warren. The details of the postoperative roentgen treatment naturally vary in individual cases, but for the most part an attempt has been made to treat this group of cases by one routine in order that we might (1) determine the results of treatment in all types of thyroid cancer with this particular method of treatment; (2) determine the amount of radiation reaction of the skin and subcutaneous tissues following this treatment, and (3) later determine the frequency of hypothyroidism following irradiation. Treatment was directed to the entire tumor bed as soon as the general condition of the patient warranted; both lobes of the thyroid gland and adjacent lymph structures in the neck, which are the most likely areas of secondary involvement, were included. The neck is divided into three portals, one on each side and one

in the midline. A total of 2,000 r was given to each portal in a period of twenty-one treatment days. It has been our experience that by treating each portal daily, thereby treating the entire tumor bed daily with cross fire radiation, a better response was obtained and there was less skin reaction and irradiation sickness following the treatment.

The following factors were used: 200 kv. (peak), 20 ma., 50 cm. distance, filter 1 mm. copper, 1 mm. of aluminum; portal 87 sq. cm., given daily to each portal, 100 r. This type of treatment gives 6,000 r to the skin, approximately 80 per cent of it being delivered to the tumor bed when a large portion of the tumor has been removed and when there has been a decompression of the muscles of the neck.

Difficulty with wound healing occurred in only one instance. In that case the difficulty came following heavy irradiation, radical operation and radon implantation in the hope of bringing about a cure in an advanced inoperable case. In this instance the wound failed to heal and there was sloughing of the skin and subcutaneous tissue.

Radiation dermatitis occurred in ten days to two weeks following treatment, the most severe dermatitis from the third to the fourth week. Healing was usually complete between the eighth and tenth weeks, with a residual bronzing and drying of the skin. During the period of active radiation reaction various ointments containing local anesthetics, such as nupercaine, were used with good effect. Telangiectasia of the skin occurred infrequently; it was a late manifestation with this type of treatment and occurred two to three years following the irradiation and in most instances has been quite mild.

Sore throat, dry throat, and hoarseness occurring during treatment and for the period of reaction were treated and controlled by aspirin gargles, with the exception of 6 cases which required cocaine sprays for relief.

In those cases in which tracheotomy was necessary, the tube was removed prior to the radiation treatment.

Follow-up. The course of the patients in the series presented was followed for a period of at least five years. Those patients who did not answer follow-up letters and those who had recurrence of the disease at the time the study was made were counted as dead from the disease (Table 1).

TABLE 1

FIVE YEAR SURVIVAL RATE IN 231 CASES OF CARCINOMA OF THE THYROID

	Per cent
Fetal adenoma	71
Papillary cystadenoma	62
Papillary adenocarcinoma	80
Alveolar adenocarcinoma	27
Small cell carcinoma	22
Giant cell carcinoma	17
Fibrosarcoma (3 cases)	33

CONCLUSIONS

The importance of the corresponding clinical and pathologic grading of thyroid tumors which allows for adequate prognosis and stands as the background of future comparisons has been reiterated, as it has been practicable for a period of twelve years.

The method and the amount of radiation necessary clinically to destroy thyroid cancers have been presented. These tumors with the exception of the giant cell carcinoma are radioresponsive, that is when 4,800 r is delivered in protracted doses clinical arrest of the disease takes place.

The reaction and the method of controlling the reaction which follows this amount of radiation have been discussed.

The five year survival of patients with all types of thyroid cancers whose course has been carefully followed over a period of five years following surgical and radiation treatment indicates the results which may be expected of the various types of thyroid cancer.*

* For discussion see page 473.

EXPERIENCES IN THE TREATMENT OF MALIGNANT TUMORS OF THE THYROID GLAND*

By U. V. PORTMANN, M.D.
Cleveland Clinic
CLEVELAND, OHIO

THIS discussion pertains to experiences with 220 consecutive cases having a diagnosis of malignant tumor of the thyroid gland seen at the Cleveland Clinic between July, 1922, and January, 1936. Approximately twice as many cases were seen by members of the staff prior to and since that time, but the series selected represents cases seen after "deep" roentgen therapy was instituted at the Clinic, and five years have elapsed since January, 1936.

The objects of the discussion will be (1) to show the relative proportion of different histological types of tumors in the series; (2) to point out the relationship of the anatomical extent of involvement according to histological types; (3) to ascertain the results obtained by surgical procedures for different types of tumors and the influence of the extent of involvement upon the results, and (4) to determine whether or not postoperative roentgen therapy has been of benefit for different types of tumors according to extent of involvement.

The series of cases was divided according to methods of treatment employed, as follows:

TABLE I

Total number	220
Recurrent	20
Primary	200
Treatment advised, none given	9
No treatment advised	20
Total primary cases treated	171
Operation alone	52
Operation, roentgen irradiation for recurrence	5
Roentgen irradiation postoperatively	79
Roentgen irradiation alone	29
Radium for recurrence	2
Radium alone	4
	171

"Recurrent" cases had operations prior to registration at the Clinic and presented themselves with local recurrence or metastases. Most of these were treated by irradiation solely for palliation; therefore, they will not be included in this study, except as they enter into the analysis of the proportion of different types of tumors when the histopathology was known. "Primary" cases are those that had had no treatment prior to registration and they are the only ones on which the results of our experience with treatment can be judged. Some primary cases had no treatment. Of these either operation or irradiation was advised for 9 patients who refused or went elsewhere and 20 patients were in such advanced stages of disease that treatment was deemed inadvisable. Cases treated by "operation alone" had total or partial thyroidectomies and a few in advanced stages and in desperate condition had only decompressions for relief of tracheal obstructions. Those listed as having "operation and roentgen irradiation for recurrence" were operated upon by Clinic surgeons but some time later were irradiated for local recurrences or metastases and, although these represent surgical failures, they are not included among the operated cases because the roentgen therapy may have modified the ultimate outcome. Cases given "roentgen irradiation postoperatively" had roentgen therapy as soon after operations as possible according to methods in vogue more than five years ago. "Roentgen irradiation alone" was given to patients in advanced stages of disease, for whom operations even for palliation were deemed inadvisable usually because of the presence of metastases. Radium was used to treat only a few cases.

* Read at the Forty-first Annual Meeting, American Roentgen Ray Society, Boston, Mass., Oct. 1–4, 1940.

Pathologists do not agree about how to classify malignant tumors of the thyroid histopathologically. The difficulty probably is due largely to the fact that the thyroid gland and most of the benign tumors (adenomata) which originate in it undergo many involutional changes that influence not only the morphology of the gland and adenomata, but probably also the character of malignant tumors in them. The histopathological classification which is used at the Cleveland Clinic is that suggested by Dr. Allen Graham, Director of the Department of Pathology. The types he has described are listed as follows:

Malignant adenoma
Papillary carcinoma
Adenocarcinoma—not originating in adenomas
Scirrhous carcinoma
Carcinoma-sarcoma
Lymphosarcoma
Fibrosarcoma
Other types of sarcoma

Malignant Adenoma. The most common benign tumors occurring in the thyroid gland are adenomas. These undergo functional and morphological changes influenced by the same or different physiological stimuli that affect the thyroid parenchyma in which they originate. Therefore, the different types of benign adenoma that occur are described according to their structure and histological variations, such as fetal, intermediate or colloid adenoma. Any one, two, or all of these transitional types may be found in a single adenoma.

Fig. 1*A*. Malignant adenoma. Thrombi of neoplastic cells protruding from veins.

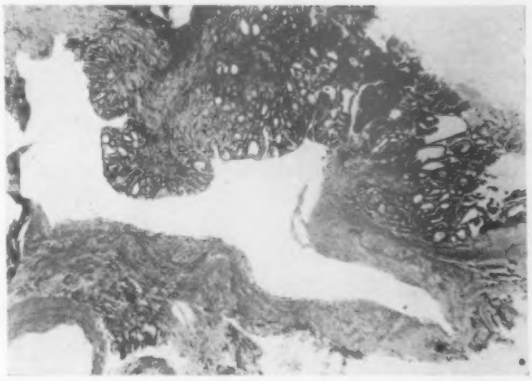

Fig. 1*B*. Malignant adenoma. Polyp of neoplastic cells attached to walls of vein.

Adenomas also become malignant; consequently malignant adenomas are the most common type of malignant tumors. As will be shown later about 90 per cent of the epithelial malignant tumors of the thyroid gland originate in pre-existing adenomas. The morphological variations or malignant adenomas are at least as numerous as those of benign adenomas in which malignant neoplasia begins. Therefore, malignant adenomas have no characteristic morphology but may have structures similar to adenocarcinoma, papillary carcinoma, medullary carcinoma, or carcinoma resembling sarcoma. Any combination of these types may occur in a single tumor.

Because of the variability in the structure of malignant adenomas it is sometimes difficult to differentiate, classify or grade them as to degrees of malignancy, or to determine their probable radiosensitivity on the basis of their histopathology alone. It is necessary to take into consideration the thyroid gland as a whole, the involutional changes which it may have undergone, the probable type of structure of the

adenoma at the time malignant neoplasia began in it, the duration of the tumor and its rate of growth, and the reaction of the stroma. However, the distinguishing characteristic of malignant adenomas, which Graham has pointed out, is that no matter what may be their morphology they invade blood vessels in which thrombi or polyps of rhous carcinoma and frank cancer; *D* is a photomicrograph of a single section of a polyp in a vein showing histopathological variations similar to those found in the tumor, namely, colloid adenoma, fetal adenoma, a structure often seen in association with exophthalmic goiter, or it might be cancer and frank cancer.

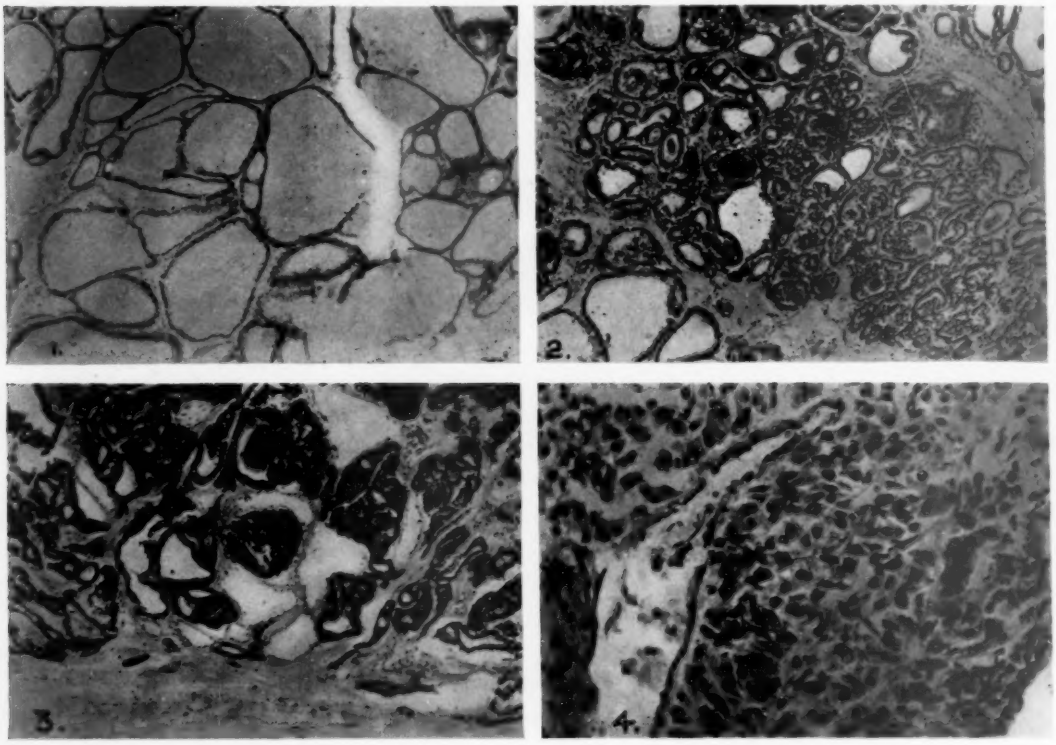

Fig. 1*C*. Malignant adenoma. Different types of neoplastic tissue from the tumor; *1*, colloid adenoma; *2*, fetal adenoma; *3*, suspicious carcinoma; *4*, frank cancer.

neoplastic cells are formed and the structure of these usually is similar to the parent tumor. The variable histology of malignant adenomas and how they invade blood vessels is illustrated by Figure 1 which shows, *A*, part of a thyroid gland containing adenomas and a large vein containing a thrombus of neoplastic cells; *B* is a low power magnification of a polyp of tumor cells attached to the wall of a small vein; *C* is a photomicrograph of the tumor showing variations in histology in a single section, these having characteristics of colloid adenoma, fetal adenoma, suspicious scir-

Papillary Carcinoma. Malignant neoplasia may begin in cystic adenomas in the thyroid gland just as it occurs in cystic tumors of other glandular organs. These tumors primarily are encapsulated and the enclosed epithelial cells are arranged in papillae (Fig. 2). As they proliferate when malignant neoplasia begins, the cells break through the thin stroma at the base of acini and invade into surrounding tissues. As would be expected from the origin and character of the growth in cysts that primarily are encapsulated, these malignant neoplasms are of a low grade of malignancy.

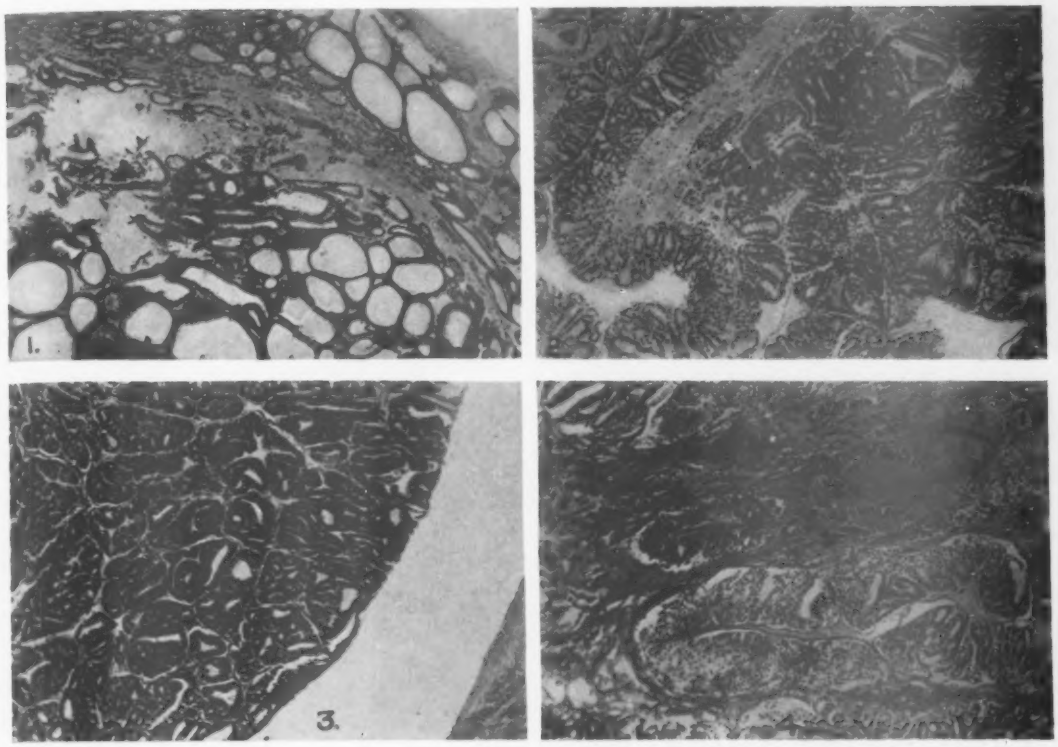

Fig. 1*D*. Malignant adenoma. Different types of neoplastic tissue from the polyp in the vein and similar to that of the tumor; *1*, colloid adenoma; *2*, fetal adenoma; *3*, hyperplastic goiter; *4*, frank cancer.

The differentiation between benign and malignant papillary tumors may depend largely upon the question of whether or not invasion has taken place rather than upon cytology. Therefore, not all papillary tumors in the thyroid gland are carcinomas, although they may have malignant potentialities. Also benign adenomas may contain areas that are papilliferous, but these should not be considered as papillary carcinomas. In addition, papillary tumors and other types histopathologically similar to thyroid tissue may occur in the thyroid and lateral aspects of the neck (lateral aberrant thyroid tumors) originating from embryonic thyroid remnants, but these seldom become malignant and are not primarily thyroid gland tumors though of the same embryological derivation.

Scirrhous Carcinoma. Scirrhous carcinomas also occur in the thyroid gland, and although it cannot be ascertained that they invariably originate in pre-existing adenomas, there is no reason why they should not do so. They have the histopathological characteristics of scirrhous carcinoma that occurs in other glandular organs with desmoplasia a prominent feature (Fig. 3).They are not encapsulated, grow slowly, and progressively by invasion of surrounding tissues through lymphatics. They destroy

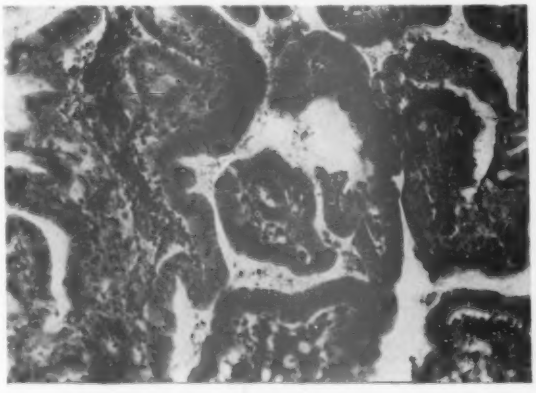

Fig. 2. Papillary carcinoma.

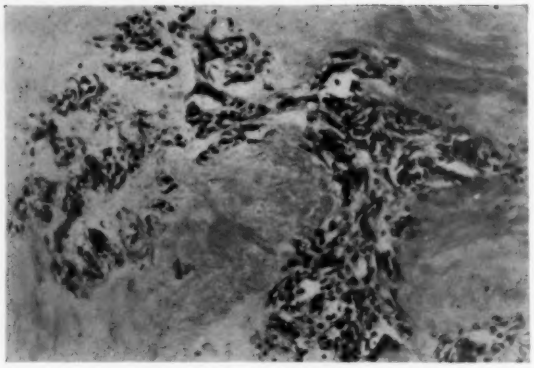

FIG. 3. Scirrhous carcinoma.

these and the life of the host by compression.

Carcinoma-Sarcoma. A very rare type of malignant tumor occurs in the thyroid gland, its epithelial elements having the characteristics of carcinoma and the stroma those of sarcoma (Fig. 4). These carcinoma-sarcomas sometimes are considered to be

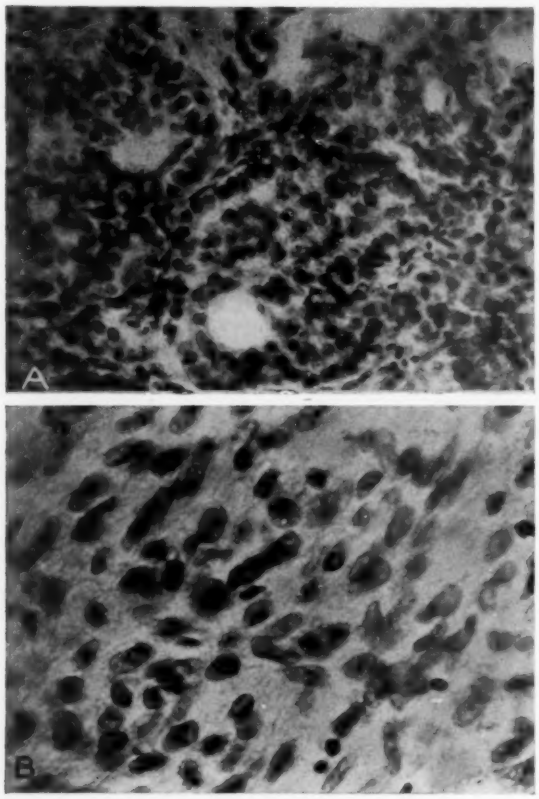

FIG. 4. Carcinoma-sarcoma. *A*, carcinoma; *B*, sarcoma.

carcinomas or fibrosarcomas, depending upon the predominant histological features. Clinically and pathologically their course is similar to scirrhous carcinomas.

Adenocarcinoma Not Originating in Adenoma. Graham called attention to these tumors recognized also by other pathologists. They appear as nodules of from microscopic size to not larger than 1.5 cm.

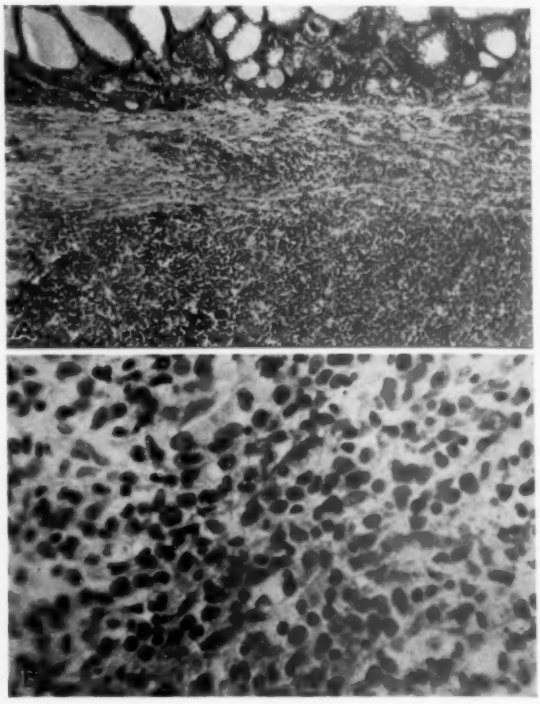

FIG. 5. Lymphosarcoma. *A*, low power magnification; *B*, high power of same tissue.

in diameter. They vary so much histopathologically that it is impractical to present illustrations of them. In many respects they resemble different types of goiter or cancer histopathologically. They are unrecognizable clinically, cause no signs or symptoms and are discovered only after removal of thyroid tissue for supposedly benign goiters; their course is unknown and in our experience no patient has developed metastases or died from this type of tumor.

Lymphosarcoma and Other Types of Sarcoma. The thyroid gland contains an abundance of lymphatic tissue and fibro-elastic

stroma in which malignant neoplasms, sarcomas, may originate. Lymphosarcomas seem to be most common (Fig. 5). Fibrosarcomas and other types of connective tissue neoplasms are rare and have the same histopathological and clinical characteristics as sarcomas of similar histogenesis occurring in other organs.

These histopathological types of malignant tumors of the thyroid gland differ in their origin or histogenesis and growth characteristics and therefore in their clinical manifestations, surgical "curability" and radiosensitivity. However, the results which can be obtained in the treatment of malignant tumors in any organs does not depend so much upon their histopathology as upon the extent of involvement at the time treatment is instituted. Therefore, when the results of treatment are to be analyzed statistically it would seem to be more important to group cases when possible according to extent or stage of growth than to classify them only on the basis of histopathological criteria which may give information about the probable rate of growth but none about the actual amount of tissue involved or distant organs that may be affected. Undoubtedly the prognosis is better for a localized tumor of any histopathological type than for one that has become too extensive to be eradicated.

Grouping cases according to extent of involvement is particularly important to radiologists who usually are called upon to treat a larger proportion of patients in advanced stages of disease than early cases. This often leads to erroneous conclusions regarding the efficacy of irradiation when the results obtained are compared with other methods, such as operations alone employed for cases in entirely different categories as regards the extent of involvement. Therefore the series of cases of malignant tumors of the thyroid gland which is the basis of this discussion have been classified according to histopathology and also grouped according to the extent of involvement determined clinically and pathologically as follows:

Group I—Cases without clinical evidence of malignant tumors of the thyroid gland, the neoplasms being small and discovered only after microscopic examination of tissues removed.

Group II—Cases without clinical evidences of malignant tumors of the thyroid gland, or their presence suspected only on the basis of the age of patients and recent rapid enlargements of goiters of long standing, or discovered at operation or microscopic examination and the tumors still localized within the capsule of the glands.

Group III—Cases with clinical or pathological evidences of malignant tumors of the thyroid gland which had invaded or extended outside of the capsules of the thyroid glands but without clinical or roentgenological evidences of metastases.

Group IV—Cases with clinical or pathological evidences of malignant tumors of the thyroid gland and also clinical or roentgenological evidences of metastases.

Table II shows the incidence of the different histopathological types of tumors in the series of cases and also the proportion of cases in each group established according to the criteria suggested as indicative of the extent of involvement.

Of all cases, 67.3 per cent were "histopathologically classifiable;" that is, the type of neoplasm could be determined microscopically. The "histopathologically unclassifiable" (7.7 per cent) had microscopic examination of tissues and the presence of malignancy was proved but the type could not be ascertained. The "total histopathologically malignant" (75 per cent) include the histopathologically classifiable and unclassifiable. The diagnosis of malignant tumor of the thyroid gland was based only upon obvious clinical manifestations in cases tabulated as "histopathology unknown" (25.0 per cent) because these were in too advanced stages of disease and had metastases, therefore operations or biopsies were deemed inadvisable so no tissues were available for microscopic examination. Although the recurrent cases in the series could not be justifiably included in the

grouping based upon extent of involvement yet the histopathological types were ascertained by examination of tissues removed at the Clinic or elsewhere, as shown in the tabulation. Only primary cases were grouped according to extent of involvement.

The percentage incidence of different histopathological types was based upon the total histopathologically classifiable. The predominating neoplasms were malignant adenomas (54.0 per cent), papillary carcinomas (14.2 per cent), adenocarcinomas not originating in adenomas (16.2 per cent) and lymphosarcomas (9.0 per cent). Others were uncommon. It is apparent that most of the tumors were of epithelial origin. If the questionably malignant adenocarcinomas not originating in adenomas are included, it will be found that approximately 80 per cent of the epithelial neoplasms originated in pre-existing adenomas (malignant adenomas and papillary carcinomas).

Only a few malignant adenomas were so limited in extent that they were placed in Group I (4.0 per cent) and about one-third (32.4 per cent) in Group II. Most of these cases were operated upon for nodular goiters and the cancer discovered after microscopic examinations of the tissues. A majority of malignant adenomas were extensive necessitating placing them in Group III (52.4 per cent) and Group IV (11.2 per cent). Most of the papillary carcinomas were still confined within their own or the thyroid capsule so that they were Group I

TABLE II

ALL CASES CLASSIFIED ACCORDING TO HISTOPATHOLOGICAL TYPES OF TUMORS AND PRIMARY CASES GROUPED ACCORDING TO EXTENT OF INVOLVEMENT

Pathological Classifications	Total Cases	Recurrent Cases	Primary Cases								Total Cases Per Cent
			Total No.	Group I		Group II		Group III		Group IV	
				No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Malignant adenoma	80	9	71	3	4.0	23	32.4	37	52.4	8	11.2	54.0
Papillary carcinoma	21	1	20	5	25.0	10	50.0	5	25.0	0	0	14.2
Adenocarcinoma not in adenoma	24	0	24	24	100.0	0	0	0	0	0	0	16.2
Scirrhous carcinoma	3	0	3	0	0	0	0	3	10.0	0	0	2.0
Carcinoma-sarcoma	1	0	1	0	0	0	0	1	10.0	0	0	.7
Lymphosarcoma	13	1	12	0	0	0	0	5	41.7	7	53.3	9.0
Fibrosarcoma	4	1	3	0	0	1	33.3	2	66.6	0	0	2.4
Myosarcoma	1	0	1	0	0	0	0	1	10.0	0	0	.7
Rhabdomyosarcoma	1	0	1	0	0	0	0	1	10.0	0	0	.7
Histopathologically classifiable	148	12	136	32	23.5	34	25.1	55	40.4	15	11.0	67.3
Histopathologically unclassifiable	17	1	16	0	0	2	12.5	10	37.5	4	25.0	7.7
Total histopathologically malignant	165	13	152	32	21.0	36	23.7	65	42.8	19	12.5	75.0
Histopathology unknown	55	7	48	0	0	0	0	9	39.6	39	60.4	25.0
Total cases	220	20	200	32	16.0	36	18.0	74	37.0	58	29.0	100.0
Per cent of primary cases				16.0		18.0		37.0		29.0		

(25.0 per cent) and Group II (50.0 per cent), but a few were extensive enough to be included in Group III (25.0 per cent). No case with this type of tumor had evidences of metastases when first seen though some died following treatment as will be shown later. All adenocarcinomas not originating in adenomas were localized and Group I cases. Other types of neoplasms were extensive when operated upon and had broken through the thyroid capsule except one fibrosarcoma.

The total percentage in each group was 16.0 per cent in Group I, 18.0 per cent in Group II, 37.0 per cent in Group III and 29.0 per cent in Group IV. This would indicate that approximately 70 per cent of the cases in the series were in advanced stages of disease when first examined, especially if patients not treated because of their hopeless condition are included in Group IV which was not done in compiling the tabulation.

In addition, there were 20 cases that were in too advanced stages of disease to be treated and therefore were not included among the primary treated cases, but should be considered as in Group IV. If these are included, then Group IV would number 78 cases and amount to 40 per cent of the total cases instead of 29 per cent.

In analyzing the results of treatment, the five year period will be used to show the numbers or percentages of cases dead and alive. There are several fallacies in this method that will be pointed out.

The "dead not of cancer under five years" died as the result of accident and cardiovascular disease and at the time had no clinical evidences of cancer. These may be justifiably deducted from the totals. It usually is difficult in analyzing five year results to deal with cases that are not traced for that long and therefore the outcome is unknown. In some statistics these cases are included among the dead and in others they are deducted from the totals. In our experience no patient with an adenocarcinoma not originating in adenoma has died of malignant tumor of the thyroid gland though 30 per cent were lost trace of and undoubtedly are still living and well. Most of the cases lost trace of had this type of tumor; therefore in this analysis the "lost trace of under five years" will be deducted from the totals. The "remaining for esti-

TABLE III

RESULTS OF ALL METHODS OF TREATMENT FOR DIFFERENT HISTOPATHOLOGICAL TYPES OF TUMORS IN PRIMARY CASES

	Malignant Adenoma	Papillary Carcinoma	Adenocarcinoma Not Originating in Adenoma	Scirrhous and Carcinoma-Sarcoma	Lymphosarcoma	Other Sarcomata	Histopathologically Unclassifiable	Histopathology Unknown	Total Cases	Per Cent Total
Total cases	71	20	24	4	12	5	16	19	171	—
Deducted										
Dead no cancer	2	2	0	0	0	0	0	0	4	—
Lost trace of	6	1	8	0	0	0	0	5	20	—
Remaining for estimate	63	17	16	4	12	5	16	14	147	100
Dead										
Under 5 yr.	43	2	0	4	8	4	14	13	88	60.0
After 5 yr.	7	1	0	0	0	0	0	0	8	5.3
Total dead	50	3	0	4	8	4	14	13	96	65.3
Alive										
With cancer	4	2	0	0	1	0	1	1	9	6.2
Without cancer	9	12	16	0	3	1	1	0	42	28.5
Total alive	13	14	16	0	4	1	2	1	51	34.7
Alive or dead of cancer after 5 yr.	20	15	16	0	4	1	2	1	59	40.0
Per cent alive or dead	31.7	88.2	100	0	33.3	20.0	12.5	7.1	40.0	—

mate" includes the "dead not of cancer under five years" and the "lost trace of under five years." The "dead of cancer under five years" and the "dead of cancer after five years" includes all cases that died unless it was definitely proved that they were clinically and roentgenologically cancer free at the time of demise, and these are included as "total dead of cancer." Patients dying in the hospital following operations or operative mortalities are included in the basis of percentage not shown in the tables.

Table III shows the results of all methods of treatment for different histological types of tumors in primary cases. After deducting the dead not of cancer and lost trace of, 28.5 per cent of cases were alive five years without cancer, 34.7 per cent with or without cancer, and 40 per cent were alive or died of cancer after that length of time. The relative seriousness of different histopathological types of tumors is shown. No pa-

Table IV

RESULTS OF ALL METHODS OF TREATMENT OF PRIMARY CASES GROUPED ACCORDING TO EXTENT OF INVOLVEMENT

	Group I	Group II	Group III	Group IV	Group I and II	Per Cent Group I and II	Group III and IV	Per Cent Group III and IV
Total cases	32	36	68	35	68	—	103	—
Deducted								
Dead no cancer	0	3	1	0	3	—	1	—
Lost trace of	8	5	2	5	13	—	7	—
Remaining for estimate	24	28	65	30	52	100	95	100
Dead								
Under 5 yr.	0	9	50	29	9	17.3	79	83.1
After 5 yr.	0	2	5	1	2	3.8	6	6.3
Total dead	0	11	55	30	11	21.0	85	89.4
Alive								
With cancer	0	3	6	0	3	6.4	6	6.3
Without cancer	24	14	4	0	38	72.6	4	4.3
Total alive	24	17	10	0	41	79.0	10	10.6
Alive or dead of cancer after 5 yr.	24	19	15	1	43	82.8	16	16.6
Per cent alive or dead	100	68.0	23.0	3.3	82.8	—	16.6	—

"dead of cancer under five years." The "alive five years with cancer" and the "alive five years without cancer" are included in the listing of "total alive with or without cancer." Cases alive without cancer for five years may be considered to be indicative of "curability" yet it is well known that the disease may recur later. The proportion of cases that live five years with or without cancer must also include those that died later of cancer and is represented by the "total lived or died of cancer after five years." In some of the tables only the numbers of cases are given in order to condense them, but the discussions may be on the tients with adenocarcinoma not originating in adenoma died of cancer. Of those with papillary carcinoma 70.6 per cent were cancer free. Of the patients with malignant adenoma, only 14.3 per cent were alive without cancer, but 3.17 per cent were alive or died of cancer after five years. The lymphosarcomas gave more favorable results since 25 per cent were well and one-third lived as long as five years, but it will be shown that this was because they responded favorably to irradiation. The prognosis for scirrhous carcinoma, carcinoma-sarcoma, fibrosarcoma and other types of sarcoma appears to be unfavorable.

Table IV shows the results of all methods of treatment of primary cases grouped according to extent of involvement. The proportion of cases that lived as long as five years is shown to be Group I, 100 per cent; Group II, 68.0 per cent; Group III, 23.0 per cent; and Group IV, 3.3 per cent. Of the all cases (29) so treated were in advanced stages of disease (Group IV) and the objective was to palliate and prolong life if possible. Neither will the results of treatment of primary cases for recurrence or those treated by radium be given because there were only a few cases. However, the results

TABLE V

RESULTS OF OPERATION ALONE FOR DIFFERENT HISTOPATHOLOGICAL TYPES OF TUMORS IN PRIMARY CASES

	Malignant Adenoma		Papillary Carcinoma		Adenocarcinoma Not Originating in Adenoma		Scirrhous and Carcinoma-Sarcoma		Sarcoma		No Histopathology		Total	
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Total cases	21	—	4	—	16	—	2	—	3	—	6	—	52	100
Deducted														
Dead no cancer	1	—	0	—	0	—	0	—	0	—	0	—	1	2.0
Lost trace of	1	—	1	—	6	—	0	—	0	—	0	—	8	16.0
Remaining for estimate	19	100	3	100	10	100	2	100	3	100	6	100	43	82.7
														100
Dead														
Under 5 yr.	14	73.7	0	0	0	0	2	100	3	100	6	100	25	58.1
After 5 yr.	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total dead	14	73.7	0	0	0	0	2	100	3	100	6	100	25	58.0
Alive														
With cancer	1	5.3	0	0	0	0	0	0	0	0	0	0	1	2.0
Without cancer	4	21.0	3	100	10	100	0	0	0	0	0	0	17	40.0
Total alive	5	26.3	3	100	10	100	0	0	0	0	0	0	18	42.0
Alive or dead of cancer after 5 yr.	5	26.3	3	100	10	100	0	0	0	0	0	0	18	42.0
Per cent alive or dead	5	26.3	3	100	10	100	0	0	0	0	0	0	18	42.0

early cases (Groups I and II) 72.6 per cent were cancer free, 79.0 per cent alive with or without cancer and 82.8 per cent lived five years. But of the advanced Group III and IV cases, only 4.3 per cent had no clinical evidences of cancer and 16.6 per cent lived five years. It is quite obvious from this tabulation that the extent of involvement of different types of tumors is an important factor which influences the results of treatment.

It is unnecessary to discuss the results obtained by roentgen therapy alone because of operations alone and of postoperative roentgen therapy will be analyzed and compared according to histopathological types and groups to try to ascertain whether or not the lives of patients may have been prolonged by irradiation. Of course, it is impossible to determine statistically whether palliation benefits have followed irradiation because there is no way to calculate mathematically varying degrees of palliation.

Table V shows the results of operation alone for different types of tumors in pri-

mary cases. Patients dying in the hospital after operation amounted to 34.6 per cent of those having operation alone and they are included among the "dead of cancer under five years." This figure does not represent the "operative mortality" in the series because many other cases had operation followed by irradiation, but the hospital deaths following operation in the total series was 13 per cent. Also most of these had palliation operations, that is, decompressions of the trachea because they were in desperate condition.

It should be noted that 5 patients were operated upon, then irradiated later for recurrences and metastases. These are not included with those having operation alone. Three of them lived over five years and 2 died in less than that time of cancer.

Table VI shows the results of operation alone for primary cases grouped according to extent of involvement. All patients in Group I who were traced were alive and well, and 71.4 per cent in Group II lived for five years. No patients in the advanced Groups III and IV having tumors that ex-

TABLE VI

RESULTS OF OPERATION ALONE FOR PRIMARY CASES GROUPED ACCORDING TO EXTENT OF INVOLVEMENT

	Group I	Group II	Group III	Group IV
Total cases	19	9	18	6
Deducted				
Dead no cancer	0	0	1	0
Lost trace of	6	2	0	0
Remaining for estimate	13	7	17	6
Dead				
Under 5 yr.	0	2	17	6
After 5 yr.	0	0	0	0
Total dead	0	2	17	0
Alive				
With cancer	0	1	0	0
Without cancer	13	4	0	0
Total alive	13	5	0	0
Alive or dead of cancer after 5 yr.	13	5	0	0
Per cent alive or dead	100	71.4	0	0

In the tabulation it is shown that the surgical "curability" of papillary carcinomas and adenocarcinomas not originating in adenomas was 100 per cent. It so happens that of the papillary carcinoma cases having operation alone all were in Group I. It will be shown in another tabulation that some tumors of this type may become extensive enough to be surgically incurable. About one-fourth (21 per cent) of the malignant adenoma cases were cancer free and 26.3 per cent lived for five years. No patients with other types of tumors lived for five years. The "curability" by operation alone was 40 per cent as represented by the "alive five years without cancer," but 42 per cent lived that long. tended outside of the thyroid capsule lived for more than a few months if operation was the only treatment.

Table VII shows the results of postoperative roentgen therapy as it was administered more than five years ago for different histopathological types of tumors in primary cases. The percentages of alive without cancer and alive or dead after five years for malignant adenomas (15.7 per cent), papillary carcinomas (69.2 per cent) and adenocarcinomas not originating in adenomas (100 per cent) is approximately the same as for these types having operation alone, but the extent of involvement is not the same in the irradiated series as those having operation alone as will be shown

TABLE VII

RESULTS OF POSTOPERATIVE ROENTGEN THERAPY FOR DIFFERENT HISTOPATHOLOGICAL TYPES OF TUMORS IN PRIMARY CASES

	Malignant Adenoma		Papillary Carcinoma		Adenocarcinoma Not Originating in Adenoma		Scirrhous and Carcinoma-Sarcoma		Lympho-sarcoma		Other Sarcomata		No Histo-pathology		Total	
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Total cases	38	—	15	—	8	—	1	—	9	—	3	—	5	—	79	100
Deducted																
Dead no cancer	1	—	2	—	0	—	0	—	0	—	0	—	0	—	3	3.9
Lost trace of	5	—	0	—	2	—	0	—	0	—	0	—	0	—	7	8.8
Remaining for estimate	32	100	13	100	6	100	1	100	9	100	3	100	5	100	69	87.3
																100
Dead																
Under 5 yr.	21	65.6	1	7.7	0	0	1	100	5	55.5	2	66.6	4	80.0	34	49.2
After 5 yr.	4	12.5	1	7.7	0	0	0	0	0	0	0	0	0		5	7.3
Total dead	25	78.1	2	15.4	0	0	1	100	5	55.5	2	66.6	4	80.0	39	56.5
Alive																
With cancer	2	6.2	2	15.4	0	0	0	0	1	11.1	0	0	0	0	5	7.3
Without cancer	5	15.7	9	69.2	6	100	0	0	3	33.3	1	53.3	1	20.0	25	36.2
Total alive	7	21.9	11	84.6	6	100	0	0	4	44.4	1	33.3	1	20.0	30	43.5
Alive or dead of cancer after 5 yr.	11	27.1	12	92.3	6	100	0	0	4	44.4	1	33.3	1	20.0	35	50.8

later. None of the patients with sarcoma lived five years following operation alone, but a few having irradiation, especially lymphosarcomas (33.3 per cent well), seem to have had their lives prolonged by the treatment. This also is suggested by the total alive or dead after five years which is 50.8 per cent for the irradiated and 42.0 per cent for those having operation alone.

Table VIII shows the results of post-operative roentgen therapy for primary cases grouped according to extent of dis-

TABLE VIII

RESULTS OF POSTOPERATIVE ROENTGEN THERAPY FOR PRIMARY CASES GROUPED ACCORDING TO EXTENT OF INVOLVEMENT

	Group I	Group II	Group III	Group IV	Group III and IV	
					No.	Per Cent
Total cases	13	26	32	8	40	—
Deducted						
Dead no cancer	0	3	0	0	0	—
Lost trace of	2	3	2	0	2	—
Remaining for estimate	11	20	30	8	38	100
Dead						
Under 5 yr.	0	7	20	7	27	71.7
After 5 yr.	0	2	2	1	3	7.0
Total dead	0	9	22	8	30	79.0
Alive						
With cancer	0	1	4	0	4	10.5
Without cancer	11	10	4	0	4	10.5
Total alive	11	11	8	0	8	21.0
Alive or dead of cancer after 5 yr.	11	13	10	1	11	28.9
Per cent alive or dead	100.0	65.0	33.3	12.5	28.9	

ease. By comparing this table with Table VI it will be noted that a higher proportion of advanced Group III and IV cases are in the irradiated series than in the ones having operation alone. There is little difference in the percentages alive in the irradiated Group I (100 per cent) and Group II (65 per cent) as compared with operation alone. However, the tabulation shows that of the advanced Group III and Group IV combined 21 per cent of the irradiated are alive and 28.9 per cent lived as long as five years while all patients in these groups that had only operation died within a few months.

It is unnecessary to give the details of the technique used in administering roentgen therapy in this series of cases. It is sufficient to state that it followed the general plan for administering roentgen therapy in vogue from 1922 to about 1935. According to modern standards the technique would be considered antequated and the dosage inadequate. This should be taken into consideration in judging the benefits that may have been derived by irradiation in this series in the light of what may be the results in future with improved technique.

SUMMARY

1. The incidence of different histopathological types of malignant tumors of the thyroid gland in a series of 220 consecutive cases was shown. The predominating types were in order: malignant adenoma, papillary carcinoma, adenocarcinoma not originating in adenoma, and lymphosarcoma. At least 80 per cent of the epithelial neoplasms originated in pre-existing adenomas.

2. The advisability of grouping cases according to the extent of disease was discussed and a plan for grouping malignant tumors of the thyroid was suggested. According to this plan approximately 70 per cent of all cases were in advanced stages of disease (Groups III and IV) when first examined and included a large proportion of the malignant adenomas, scirrhous carcinomas, carcinoma-sarcomas, lymphosarcomas and other types of sarcoma. The types that were early and localized (Groups I and II) were a few malignant adenomas, most papillary carcinomas and all adenocarcinomas not originating in adenomas. The fact that no patient with the latter histopathological type of tumor died of cancer suggests that they should not be considered as malignant tumors of the thyroid gland except histopathologically.

3. According to tabulations of results and comparison of those obtained by operation alone and by postoperative roentgen therapy, no benefits were noted from irradiation of patients with tumors still localized within the thyroid capsule (Groups I and II) but the irradiation probably prolonged the lives of some patients with extensive involvement from malignant tumors of the thyroid gland (Groups III and IV).*

* For discussion see page 473.

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RADIOACTIVE IODINE AS AN INDICATOR IN THYROID PHYSIOLOGY

OBSERVATIONS ON RABBITS AND ON GOITER PATIENTS*

By SAUL HERTZ, M.D.
BOSTON, MASSACHUSETTS

THIS report summarizes a series of cooperative experiments started in the fall of 1937, on the metabolism of iodine in relation to thyroid function. The only radioactive isotope of iodine then available was I^{128}, with a half period of twenty-six minutes. The earliest experiments[1] demonstrated that the collection of iodine by the thyroid was extremely rapid, the amount present in the gland within ten minutes after intravenous injection not being exceeded within ninety minutes. Hyperplastic glands collected more iodine than did normal glands, the injections being equal.

A systematic study was then undertaken of the relations among the dosage of administered labelled iodine, the time of collection, previous iodine administration, and the functional state of the thyroid as indicated by its size. The results[2] indicated that the thyroid took up a larger portion of a small dose of iodine than it did of a large dose. Curves showing these relations were established for normal animals, animals treated with anterior pituitary thyrotropic hormone, animals on an exclusive cabbage diet, and animals injected with methyl cyanide. Previous iodine administration caused a marked decrease in the collection of subsequent doses.

When strong samples of the newly discovered long-lived isotopes of iodine became available, further lines of investigation were undertaken. These were the extension of experiments on thyroid iodine collection to patients with Graves' disease, the chemical investigation of the partition of iodine among various iodine fractions in the thyroid, and the introduction of a new technique, multiple labelling,[2] for the study of different doses of iodine at the same time. The multiple labelling technique showed that the collection from a second dose of iodine is almost invariably less than that from the first dose. This led to the suspicion that the routine preoperative massive iodinization in Graves' disease might be unnecessary. It has now been shown that the response to a single dose is clinically indistinguishable from the response to protracted iodinization.

At the same time a more complete correlation of iodine collection with the known measures of thyroid function, viz., basal metabolic rate, thyroid size, histologic appearance, and with the time and method of preparation of the subject was carried out using rabbits. The experiments upon patients with Graves' disease were at first concerned with measuring the amount of iodine in the thyroid (as obtained at operation) which remained from a single initial labelled dose of varying size, administered at various times during the course of iodinization and at varying intervals before operation. In addition, the chemical fate of the iodine was investigated, and the urinary excretion followed. As in rabbits, maximum collection was found within a short time after administration, and collection was relatively largest from small doses of iodine. Chemical analysis in the main confirmed previous findings.

In a recent series of experiments, an externally placed counter was used to measure the relative activity of labelled iodine in the thyroid as a function of time. By means of a single absolute determination after surgery, it was possible to calculate the absolute content at any previous time. *The initial thyroid collection in previously untreated Graves' disease patients approxi-*

* From Massachusetts General Hospital, Massachusetts Institute of Technology and Harvard Medical School. Read at the Forty-first Annual Meeting, American Roentgen Ray Society, Boston, Mass., Oct. 1–4, 1940.

mates 100 per cent for small doses (0.2–5.0 mg.), while the initial collection of previously iodinized patients, normal controls, and the collection of all patients from larger doses is considerably smaller. These results are not inconsistent with the smaller collections obtained by Hamilton and Soley[3] from larger doses. This initially collected iodine rapidly leaves the thyroid in the untreated patients given small doses, less than a third remaining after a week, with a slower decline thereafter.

A series of experiments on the behavior of thyroids isolated and surviving in a perfusion apparatus has been instituted; and it has been shown that the behavior of the thyroid in collecting iodine from the perfusion fluid is directly comparable to the results in vivo.[4,*]

REFERENCES

1. Hertz, S., Roberts, A., and Evans, R. D. Radioactive iodine as indicator in study of thyroid physiology. *Proc. Soc. Exper. Biol. & Med.*, 1938, *38*, 510–513.
2. Hertz, S., Roberts, A., Means, J. H., and Evans, R. D. Radioactive iodine as indicator in thyroid physiology; iodine collection by normal and hyperplastic thyroids in rabbits. *Am. J. Physiol.*, 1940, *128*, 568–576.
3. Hamilton, J. G., and Soley, M. H. Studies in iodine metabolism by use of new radioactive isotope of iodine. *Am. J. Physiol.*, 1939, *127*, 557–572.
4. Mainini, C. G. Personal communication.

* For discussion see page 473.

CARCINOMA OF THE THYROID*

By FRANK H. LAHEY, M.D.
Department of Surgery, The Lahey Clinic
BOSTON, MASSACHUSETTS

IN ANY discussion of cancer of the thyroid from a surgical point of view the outstanding points of interest must naturally be directed to the questions (1) do lesions of the thyroid exist as benign tumors and later become malignant, and (2) how may one recognize cancer of the thyroid early so that combined surgery and irradiation may be applied to it with the possibility of a cure?

There are but few dissenters today from the opinion that most cancers of the thyroid originate in a lesion which is primarily benign, remains benign for some time and later becomes malignant, that is the discrete fetal or embryonal adenoma. This is important to stress and restress particularly to roentgenologists who are having these cases sent to them, to medical men who are expressing opinions that they are cysts or that they are harmless and do not require treatment, and to surgeons whose interest and experience with thyroid tumors has been so limited that they are not acutely aware of the danger of malignant degeneration in these tumors.

One has only to see such a case as will be briefly described to have indelibly impressed upon his mind the desirability of removing these discrete adenomas even though the percentage of malignant degeneration in them is relatively low.

CASE REPORT

A young girl in college came to the Clinic on June 23, 1937, because of an enlargement in her neck which she had had for three years. This had been known by her medical advisers, and she had been repeatedly told that since it gave her no trouble it did not require removal. This advice was given by an outstanding medical consultant. This is not said critically but with the hope that it will have educational advantages. Examination showed that she had a firm, smooth, round adenoma, the size of an English walnut, which could be felt in the lower left pole extending beneath the sternum. She came to the Clinic because this had slipped beneath the sternum and now, as she bent over, caused pressure. Had this mechanical pressure on the trachea not occurred she undoubtedly would still have been advised not to have it removed.

On June 25, 1937, this adenoma was removed. The pathologic report was carcinoma, partly papillary, partly small cell type. She was discharged seven days after operation and a series of twenty-three intense radiations, 7,000 r being delivered to the thyroid gland, was given by Dr. Hare. The patient married and remained well until March, 1939 (one year and ten months), when she returned to the clinic because of headaches which had become severe within the past three weeks. There were no signs of local recurrence. Because of the headaches, on May 1 right cerebral craniotomy was performed by Dr. Horrax of the Neurosurgical Department of the Clinic, with the excision of a segment which on pathological report proved to be metastases from the carcinoma of the thyroid. This patient died on May 27, 1939.

With no purpose of being critical but in order that I may stress particularly for roentgenologists who may see these cases at first hand the dangers of this lesion, this case is cited. Had this patient had the small adenoma of the thyroid removed three years previously when it first appeared she would undoubtedly be alive and well today.

We have now operated on over 19,500 goiters. In this experience have been many patients with adenomas, among whom this episode has repeatedly occurred. It is therefore our urgent desire as a contribution to the problem of cancer of the thyroid to stress and restress that the outstanding need in this situation is an appreciation of the danger of malignancy in discrete adenomas, the fact that their removal by those

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experienced in thyroid surgery presents no risk whatever, and that if discrete adenomas are removed when they are first discovered, regardless of their size and regardless of the age of the patient, the problem of cancer of the thyroid will be more adequately controlled than if we approach this lesion after the diagnosis has been well established by means of the combined irradiation and surgical treatment.

There is a tendency on the part of those who have not had a large experience with the thyroid to make two wrong assumptions regarding these discrete thyroid tumors. One is that if the tumor is small there is little danger of its being malignant, and second, if it is in a young person there is likewise little danger of malignancy within the tumor. Based upon our experience, neither of these assumptions is correct. We have seen an adenocarcinoma in an adenoma of the thyroid no larger than one's thumbnail, and we have seen carcinoma of the thyroid occur in a child nine years of age, resulting fatally. We have again and again seen it at twelve, fourteen, fifteen and sixteen years. It is therefore unsafe to assume that a tumor of the thyroid may not be malignant either because it is small or because it occurs in a young person.

It is important, particularly for the roentgenologist, to be familiar with some of the clinical evidences of malignant degeneration in an adenoma of the thyroid. While one cannot say that all discrete adenomas of the thyroid which are not firm are not malignant, exclusive of those tumors of the thyroid into which hemorrhage has occurred, firmness within an adenoma of the thyroid is extremely suspicious evidence of malignant degeneration within the tumor. Any change, therefore, in the consistency of the tumor should make one extremely suspicious of the possible presence of malignant degeneration within the capsule. Since discrete tumors of the thyroid, or discrete adenomas of the thyroid, are encapsulated with a definite, thick fibrous capsule, they are discrete in outline. When malignant degeneration occurs and penetrates and erodes this fibrous capsule, the discreteness of outline of such a tumor is lost. Any changes, therefore, in outline of a discrete adenoma of the thyroid should make one extremely suspicious of malignant degeneration within the tumor.

Adenomas of the thyroid, being discrete, are as a rule movable. When such a tumor becomes fixed, this fixation is usually due either to exudate about the tumor secondary to hemorrhage into the tumor or to malignant degeneration with perforation of the capsule and fixation of the tumor to the trachea or surrounding structures. Loss of mobility, therefore, in any tumor of the thyroid which has previously been mobile is also an indication of malignant degeneration within an adenoma.

When a discrete adenoma has existed within the thyroid gland over a considerable period of time with no change in the voice, and the voice then becomes husky and laryngeal examination shows paralysis of the recurrent laryngeal nerve on the same side as that lobe in which the tumor exists, one should be extremely suspicious of malignant degeneration penetrating the capsule and involving the recurrent laryngeal nerve in the growth.

One of the most confusing thyroid diseases to differentiate from cancer of the thyroid is thyroiditis of the Riedel struma type or of the Hashimoto type. This is confusing because thyroiditis produces a change in consistency of the thyroid gland to that of almost stony hardness. Because everyone is suspicious of cancer of the thyroid in the presence of marble-like hardness, in cases of thyroiditis a diagnosis is often made of carcinoma of the thyroid, particularly when one lobe is large, firm and fixed. The outstanding difference between thyroiditis and cancer of the thyroid is that in thyroiditis the thyroid is of stony hardness but its anatomical outline is completely retained. There may be enlargement of the thyroid lobes but they retain their normal contour, with sharp points where the superior thyroid artery enters, with a definite isthmus and with definite and normal outlines of the

body of the thyroid. On the other hand, since most cancers of the thyroid start in a discrete adenoma, the swelling in this state is often unilateral, it is often local and the contour of the thyroid is lost. Thyroiditis, on the other hand, usually involves the entire thyroid throughout both lobes, the stony hardness being diffused through the entire gland. With thyroiditis, the entire gland, in addition to being markedly indurated, is frequently so firmly fixed that it is impossible to lift the lateral lobes digitally out of their beds. This is due to the inflammatory exudate about the thyroid itself. Another suggestive factor in cancer of the thyroid is that lymph nodes are involved relatively early while with thyroiditis, even in the presence of induration of the entire thyroid gland, lymph node enlargement is rare.

It is extremely important to differentiate between cancer and thyroiditis as already stated, because of the similarity in the consistency of the thyroid in both conditions. In thyroiditis, however, cancer practically never develops in relation to the thyroiditis; the only symptoms are those related to the diminished thyroid secretion secondary to the round cell infiltration of the gland and occasional constrictions of the trachea due to organization of the inflammatory exudate within the thyroid. The differentiation is particularly essential since in thyroiditis surgery is rarely necessary and in cancer of the thyroid it should be instituted early.

There is still another type of thyroid tumor which should be impressed upon the minds of everyone dealing with abnormal conditions of the thyroid; that is, lateral aberrant bodies. I am sure that we have seen more mistakes in diagnosis made with this type of thyroid tumor than with almost any other of the thyroid enlargements.

Everyone is familiar with the fact that the main origin of the thyroid gland is represented by the foramen cecum as a remnant of the point where the thyroid originates in the base of the tongue, that it descends from this position to its adult location on the trachea. Some are not familiar with the fact that there are occasionally lateral thyroid origins from the ultimo-branchial bodies, growing in from the side, which produce the gland-like masses of thyroid tissue well outside the thyroid itself and running laterally up and down the course of the internal jugular vein. These are the so-called lateral aberrant thyroid bodies and it is to this group of cases that I particularly wish to call attention.

In any patient having longitudinally distributed sets of gland-like masses running up and down either on one or both sides of the neck in front of the sternomastoid muscles in relation to the internal jugular, when they are discrete and noninflammatory, one should be extremely suspicious of the possibility that they are the papilliferous lateral aberrant thyroid bodies. It is particularly important to have these in mind because of the fact that they all possess possibilities of malignancy within them. They are often filled with blood pigment escaping from the papilliferous elements within the tumor and so when surgically exposed, are often blue or black in color, giving them an appearance not unlike that of melanotic sarcomas.

There is another feature concerning these lateral aberrant thyroid bodies about which we feel reasonably sure but not certain, and that is that they can metastasize directly into the thyroid gland itself. It is certain in our experience that we have at times removed these primary lateral aberrant thyroid bodies from both sides of the neck and found nodules of a similar microscopic character within the thyroid gland.

The danger of this situation is well illustrated by several cases which have occurred in our experience in which the nodule within the gland was removed surgically, submitted to a pathologist not widely experienced with thyroid pathology, and a report of cancer of the thyroid returned. In such cases it has more than once been assumed by the surgeon and by the roentgenologist treating the case postoperatively that the lateral gland-like structures were

metastases and that the case was hopeless from a surgical point of view and therefore to be treated solely by irradiation. In many of these cases the direct reverse of the interpretation of the situation has been true. The origin of the tumor was in the lateral aberrant thyroid bodies, which had metastasized to the thyroid gland and the removal solely of the discrete tumor within the thyroid resulted in leaving behind masses of epithelial thyroid tissue in the form of the lateral aberrant thyroid bodies in which malignant degeneration could or already had taken place.

The treatment of lateral aberrant thyroid masses is their complete removal by surgical operation; complete dissection of the gland-like masses from the clavicle well up to the angle of the jaw, together with removal of any implantations within the thyroid itself. Since this type of thyroid tumor is extremely radiosensitive these cases should all be followed by intense irradiation, with an excellent prospect of nonrecurrence.

We have now operated upon 34 patients for lateral aberrant thyroid bodies, and of this group malignant degeneration had already occurred in 35 per cent. Of the entire series treated by radical surgery and irradiation, 1 patient died of recurrence and 3 are living, with recurrence of the cancer.

TREATMENT

One should not discuss the question of cancer of the thyroid, I feel sure, without discussing the question of treatment. Until a few years ago everyone's attitude toward the management of cancer of the thyroid was quite pessimistic. Previous to that, the surgical approach to the treatment of thyroid cancer was that of attempting to remove the entire thyroid gland. With the establishment of better cooperation between the radiologist and the surgeon and a better understanding of the entire situation of cancer of the thyroid, much more satisfactory and gratifying results have now been obtained. The present day treatment of cancer of the thyroid is by no means hopeless, as will be shown in the group of five year nonrecurrence rates shown in the different grades of cancer of the thyroid (Table 1).

Since you as radiologists will have occasion to deal with the problem of cancer of the thyroid, primary and recurrent, in which the additional factor of surgery must at times be advised, it is important for you to know a little something about the surgical treatment of cancer of the thyroid.

Table I

CARCINOMA OF THE THYROID
FIVE YEAR SURVIVAL RATE, 231 CASES

	Per Cent
Adenoma with blood vessel invasion	71
Papillary cystadenoma, malignant	62
Papillary adenocarcinoma	80
Alveolar adenocarcinoma	27
Small cell carcinoma	22
Giant cell carcinoma	17
Fibrosarcoma	33

It has proved relatively unsatisfactory to attempt to deal with cancer of the thyroid solely on the basis of attempts to ablate the thyroid completely, together with all of its malignant cells. This is due to the fact that lymph nodes are involved relatively early in this disease and the structure of the thyroid, situated as it is so close to numerous other structures and so adherent to the trachea, does not lend itself, as for example cancer of the breast does, to the removal of wide margins of unaffected tissue about the tumor. It is for this reason that practically everyone has managed cancer of the thyroid by means of combined surgical and radiation therapy.

No surgical operation should be undertaken on cancer of the thyroid without realizing that one of the characteristic features is its tendency to involve venous channels and to extend along them. It is for that reason that when cancer of the thyroid is managed surgically not only should the entire lobe of the thyroid involved be removed, but all of the tributary branches of the thyroid veins running to the internal

jugular vein, together with a high and low section of the internal jugular should be removed with the tumor.

We are all very much indebted to Dr. Allen Graham, of the Cleveland Clinic, who has stressed this point. He has particularly called attention to the fact that should a recurrent nodule of the thyroid occur in spite of irradiation, in which surgery seems indicated, local removal of such a nodule is unsound surgery. The surgical approach to such a recurrent nodule should include wide removal of the internal jugular vein and all veins adjacent to this nodule, together with all of the overlying adherent muscle and thyroid tissue.

SUMMARY

It has been my purpose to make this discussion a practical presentation of the types of tumor in which cancer of the thyroid occurs, to stress the necessity of removing the benign fetal and embryonal adenomas before they become malignant, and to discuss the clinical evidences of the occurrence of cancer within these adenomas. I have, in addition, attempted to present some of the differentiating points between the condition most often mistakenly diagnosed cancer, that is thyroiditis, and to discuss the clinical features and dangers of cancer in lateral aberrant thyroid bodies.

The principles involved in the surgical treatment of cancer of the thyroid are stated.

DISCUSSION OF SYMPOSIUM ON CLASSIFICATION, TREATMENT AND PROGNOSIS OF CARCINOMA OF THE THYROID*

Dr. A. C. Christie, Washington, D. C. I am sure these very interesting papers have left us with a definite conviction of the importance of this field and of its difficulties.

It is evident there is still a great deal of difficulty with regard to the classification. I find Dr. Warren's classification very helpful. We all share, I am sure, his expressed wish to make it more simple as time passes. The difficulties are immediately apparent in the field of pathology. Many thyroids are removed, small adenomas found within them, and on examination of that adenoma there is found evidence of malignancy when there was no such evidence beforehand clinically. Dr. Portmann has emphasized this point by the slide he showed representing different types of histological tissue not only in the same thyroid gland but also within one very small papillary nodule within the gland.

Similar difficulties are apparent in the clinical field. The terms carcinoma-sarcoma and myelolympho-sarcoma illustrate these difficulties. It is difficult or impossible in certain cases to say whether a tumor is a highly cellular carcinoma or one which belongs to the lymphomatous type.

The difficulties are still further emphasized in the field of diagnosis. It is often impossible to determine whether a given tumor is benign or malignant. It is for this reason that Dr. Lahey has emphasized the importance of surgical removal of all of these tumors.

In the field of radiation treatment, Dr. Warren and Dr. Hare have called attention to an important difference in response of the papillary and alveolar types of tumors. The papillary type responds readily to irradiation so that we may expect good results after application of about 4,800 r while the alveolar type is much more resistant and requires dosage up to the limit of tolerance.

Dr. Portmann's classification based upon the stage of the disease seems to me important from the radiologist's standpoint. Cases in Stage I have a high percentage of cures by surgery and it is doubtful whether irradiation has any additional advantage. In Stages II and III, however, Dr. Portmann has shown by his statistics that irradiation offers distinct advantages and that the percentage of cures can be considerably increased by its use.

Dr. Hare (closing). I wish to thank Dr. Christie for his excellent discussion of our paper, and to answer his question. We plan to give 6,000 r to the skin of each patient being treated, which delivers 4,800 r to the tumor bed; that is, we plan that at least 80 per cent of the radiation will extend at least 2 cm. beneath the skin.

As Dr. Lahey has pointed out, in each case when malignant change is known to be present at operation, a radical operation is done, with removal of the muscles and veins of the neck. This leaves very little tissue between the skin

* Papers by Drs. Warren, Hare, Portmann, Hertz and Lahey.

and the trachea, and the depth dose we should get by this method will give a very high dose to the tumor bed. The basis of my figures is on the dose delivered to the tumor bed and not to the skin.

Dr. Hertz (closing). The incidence of nodules in the thyroid at postmortem on routine examination of patients may run as high as 16–50 per cent at different age groups. This was carefully done by Dr. Schlesinger in Boston, at Beth Israel Hospital. There is a pertinent fact: If we are to remove every nodular goiter for the prevention of neoplasms later in life, I think we would have to remove up to 50 per cent of all the thyroids in the City of Boston or more in certain other cities. If Dr. Lahey would do that personally, or if men did it who were equally trained and equally equipped to do such an operation, I would not, even then, be all in favor of it. But, on the other hand, with all deference to Dr. Lahey's opinions and his surgical skill, I feel in my own mind (and I am speaking only for myself, on the basis of a large thyroid experience) that surgery as it is done in smaller cities, towns, and hamlets, should not be done on these nodular goiters without thinking more than twice about it.

I have seen the complications of thyroid surgery. I do all the follow-up work at the Massachusetts General Hospital, on the thyroid cases of men who are adequately trained; and also see the misery coming into the clinic from other parts of the country, from the outlying districts of New England and also, I am sorry to say, from our own City of Boston occasionally. On that basis I believe it is very important for us to adopt an attitude that unless we have a very good reason for removing a thyroid, we should not remove it!

Now as to the danger of cancer. Will a little lump in the thyroid eventually go on to malignancy and kill the patient? Obviously the outlook even if cancer has developed in *its earliest form, under observation*, is very good, either from total removal, as Dr. Lahey has stated, with resection of the veins in the cases that need it, and irradiation in those cases that have recurrence, or in whom the removal seems not to have been complete because of mechanical considerations. This was the sense of the papers on today's program.

Next, there is the question of whether, granted you did remove the "adenoma" or nodule of the thyroid, which appealed to you as being particularly prone to become maligant eventually—does that offer an adequate prophylaxis against the development of other nodules and other local foci that "might become malignant" just as the one that you had originally suspected might be becoming malignant?

I am writing this up as an editorial because of the possibilities inherent in too much surgery being done at the advice of men who have the enthusiasm of preventing cancer by these "prophylactic operations on the thyroid gland"—I feel that the following points need to be stressed, and stressed over and over again:

One side of the question has already been expressed, that of being on the wary side and being worried about these nodules, and following and watching them, and being sure you see the patient. Don't let the patient go away to college for three years and not see her again,and say, "Well, that is all right. We will pass that by and we need never worry about that," as seems to have been done in the case of Dr. Lahey's young patient.

The thing to do in any of these cases is to observe the nodule, see what its biologic characteristics are, what its descriptive manifestations are, and see if it changes in any period of time. If changes do take place, then we should remove such nodules with dispatch.

Of the 35 cases of which I have records in my desk at the present time there are 5 cases which have had up to four operations on the thyroid gland for the removal of cysts, nodules, calcified lumps in the thyroid, and finally ended up with a definite diagnosis of carcinoma of the thyroid. I have selected these 35 cases out of a group of 50 cases of malignant goiter at the Massachusetts General Hospital, as a text for this virtual sermon. *With multiple operations on these thyroids, cancer has developed despite the "prophylactic surgery."* That they were not cancer originally is attested to by the fact that the average duration of the goiter in these cases was so long. The dates of the first operation were as long as twenty years previous to the development of cancer of the thyroid!

Dr. Lahey (closing). I wish to restate my opinion that all discrete tumors or adenomas should be removed. This statement might be misinterpreted to mean that every patient with an enlarged nodular goiter should be operated upon, which is not what I advise. If I lived in a region where goiter is endemic I would agree with Dr. Hertz that I would be busy night and

day. This type of thyroid enlargement should in no way be confused with the discrete adenoma. Dr. Shields Warren has pointed out that in endemic goiter the so-called colloid adenomatous nodules are in all probability not true tumors but local areas of hyperinvolution with fibrous capsules. In these there is not the danger of subsequent malignancy that there is with the discrete tumor or adenoma.

If you are a medical man and not facing the decision as to advising operation with the direct responsibility for protecting these patients from the development of cancer, the problem may not seem so acute as it does to me. I have seen many patients who have been previously advised that no operation was necessary for the small adenoma of the thyroid who subsequently developed cancer which in some cases was then inoperable.

It is poor judgment to wait until the diagnosis of cancer can be made clinically and it is impossible to tell when these tumors will undergo malignant degeneration.

If Dr. Hertz will admit that cancer develops in some of these adenomas, he should agree to their removal if the operation can be done with little risk. From my experience, I can assure you that this can be done and I wish finally to emphasize the importance of the removal of all discrete tumors of the thyroid.

ROENTGENOLOGICAL DIAGNOSIS OF PRIMARY CARCINOMA OF THE LIVER*

By RICHARD SCHATZKI, M.D.
BOSTON, MASSACHUSETTS

PRIMARY carcinoma of the liver is generally thought to be a rare disease, and in the differential diagnosis of malignant tumors this lesion is usually not considered as a possibility. In 4,323 autopsies performed in the Pathological Department of the Massachusetts General Hospital within the last thirteen years, 15 cases of primary cancer of the liver were found, that is 0.34 per cent of all autopsies. This incidence is similar to that reported in the literature (Charache,[7] Greene,[11] Gregory,[12] Gustafson[13]). It is interesting to find that carcinoma of the pancreas, a tumor which is frequently thought of as a primary source of malignancy, is only about three times more common than primary cancer of the liver in the autopsy material of the Massachusetts General Hospital. Primary cancer of the liver, while not a common disease, should therefore not be classified as a rarity.

The clinical diagnosis of a primary tumor of the liver is difficult, and it is made in only a small percentage of cases (Greene,[11] Gregory[12]). It has been our experience that roentgenological examination may at times be of help in the diagnosis. Since the roentgen findings are based on the somewhat unusual anatomical characteristics of the tumor, a review of the pathological findings is necessary.

Eggel[8] divided the primary carcinomas of the liver grossly into three types: (1) a nodular type in which one or several discrete nodules of varying sizes are found; (2) the massive type in which the tumor mass involves an entire lobe, or the larger part of a lobe; and (3) the diffuse type which may be impossible to differentiate from cirrhosis of the liver grossly. The second type is of particular interest to the roentgenologist because it frequently appears as a single large mass protruding considerably from the surface of the liver.

Histopathologically, the tumors, with few exceptions, are easily differentiated into those which arise from the liver cells proper, the "hepatoma," and those which originate from the intrahepatic bile ducts, the "cholangioma" or primary adenocarcinoma of the liver. Metastases are fairly common in both types, the liver, the periportal lymph nodes and the lungs being most frequently involved. Large tumor thrombi in the hepatic veins and in the inferior vena cava are not uncommon.

Of great theoretical and practical importance is the common association of primary liver cell carcinoma with cirrhosis of the liver. This was noted by early investigators and has been confirmed in later publications. Eggel[8] found cirrhosis to be present in 85 per cent of all hepatomas and in 50 per cent of all cholangiomas. Jaffe[14] found 7 liver cell carcinomas occurring in 85 cases of cirrhosis, Loesch[16] saw 14 in 94 cases of cirrhosis. Steiner[21] collected 77 cases of primary cancer of the liver in children. This group is quite distinct from the tumors in adults. Cirrhosis is rarely ever found in this group and a congenital origin is suggested.

In the 15 autopsied cases observed in the Pathological Department of the Massachusetts General Hospital during the last thirteen years, 11 were found to be hepatomas, 4 to be cholangiomas. Ten of the 11 cases of hepatoma were associated with cirrhosis, the exception being in a woman, aged seventy-eight, the only female of the hepatoma group, and the only one without cirrhosis. Of the cholangiomas, 3 showed cirrhosis and one did not.

Only a few brief remarks on the roentgen findings in primary carcinoma of the liver are scattered throughout clinical reports in the literature. They consist largely of descriptions of the deformities produced by

* From the Department of Roentgenology, Massachusetts General Hospital, Boston.

general or localized enlargement of the liver. Schnabel,[20] Strong and Pitts,[22] as well as Liber and Brown,[15] mentioned a high right diaphragm, the movements of which were restricted in Schnabel's case. In Novati's[18] case the diaphragm was pushed upward by nodules which increased rapidly in size during successive examinations. Displacement of the stomach, duodenum, small intestine or colon was found in a number of other cases.

Roentgen examination with the aid of artificial pneumoperitoneum has been recommended as a means of demonstrating pathological masses in the region of the liver. After the insufflation of air into the peritoneum in Novati's case, polycyclic shadows on the lateral and lower surfaces of the liver were visible.

A few authors have advocated the use of thorotrast for the diagnosis of primary tumor of the liver (Ehrlich and Ansanelli,[9] Novati[18]). The results in these cases were not quite as successful as one might expect. In the case reported by Ehrlich and Ansanelli, a picture resulted which was similar to multiple metastases in the liver, while in Novati's case an adequate demonstration of the liver was prevented by the extensive destruction of the reticulo-endothelium of the liver. The possibility of late damage following the intravenous injection of this radioactive substance is still unsettled. There is enough doubt in the minds of the majority of roentgenologists to prevent its general use. It is very likely that the use of a more acceptable radiopaque substance would be of help in the diagnosis of primary cancer of the liver. It is too early to decide whether or not the new colloidal organic iodine compounds recommended by Beckermann and Popken[2] will adequately serve this purpose.

In summary, the roentgenological evidence of primary cancer of the liver as reported in the literature is meager and not at all characteristic. Boyce and McFetridge,[3] in reporting 24 of their own cases conclude that "the x-ray gives surprisingly little assistance and may be quite misleading."

Our interest in the roentgenological manifestations of primary carcinoma of the liver began with the study of a case in which we were able to make a correct diagnosis on roentgenological evidence only. We believe that the diagnosis was made on reasoning that will be useful again in similar cases.

Case 1 (Case Records of the Massachusetts General Hospital; Case 23051)[5] (Figs. 1 and 2). An American engineer, aged sixty-two, was admitted complaining of a mass in the abdomen and a cough. Patient had been a known syphilitic for thirty-six years and had been treated with mercury and arsphenamine. About eight weeks before entry he developed a dry hacking cough, which became paroxysmal in character five weeks before entry. Examination by his physician showed a mass the size of a small grapefruit in the mid epigastrium and considerable abdominal distention. Roentgen studies of his gastrointestinal tract were found to be negative in another hospital. After discharge from this hospital the mass increased in size, and the abdomen became progressively distended. Six years before admission to the Massachusetts General Hospital he had had jaundice, details of which were not known.

On admission to our hospital he was dyspneic and slightly undernourished. The abdomen was markedly distended and tense. There were tympany in the region of the umbilicus and slight shifting dullness in the region of the flanks. In the mid epigastrium extending half way to the umbilicus was a stony hard, lobulated mass. Hinton test was negative. Guaiac test gave a 1+ reaction. Roentgen examination of the chest showed mottled dullness in both lung fields, less pronounced at the apices. The mottling consisted of foci ranging from a few millimeters up to 0.5 cm. in diameter. They were hazy in outline and in some places confluent. Gastrointestinal series demonstrated extensive varices involving almost the whole thoracic portion of the esophagus. The stomach was displaced to the left by a soft tissue mass, the center of which was at the level of the spine corresponding to the position of the left lobe of the liver. The right lobe of the liver was not enlarged, and appeared if anything smaller than usual. The first portion of the duodenum was unusually long and reached high into the right hypochondrium where there was an unusual amount of gas filled loops of small and large intestine.

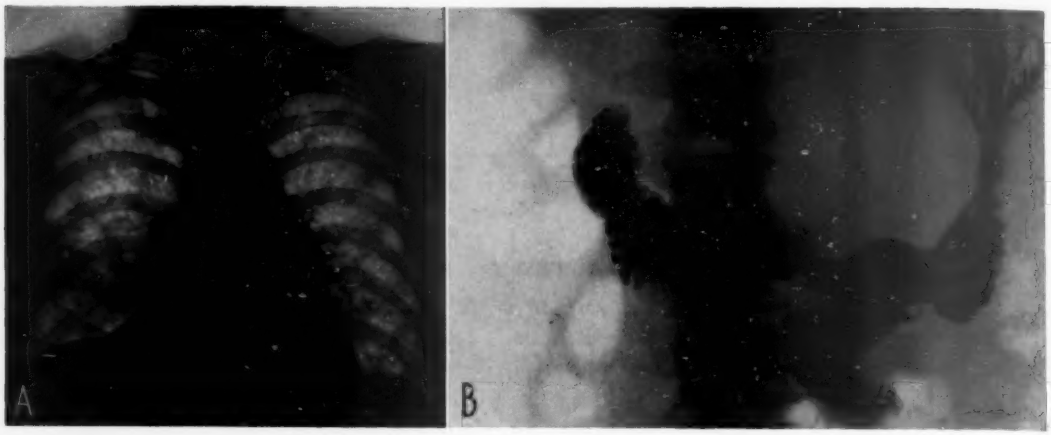

Fig. 1. Case 1. Primary carcinoma of the liver with metastasis to the lungs. *A*, mottling in both lung fields produced by numerous metastases. *B*, displacement of the stomach by a large mass in the left lobe of the liver. The right lobe of the liver is small as can be seen from the high position of the duodenum and of the air-filled small intestine.

The roentgen diagnosis was that of primary carcinoma of the left lobe of the liver superimposed on cirrhosis of the liver, multiple lung metastases. The patient's condition became progressively worse. Despite the fact that the abdomen was tapped and fluid removed, distention returned very rapidly, and the patient died on the fourth hospital day.

At autopsy the liver was found to weigh 2,200 grams. The surface was coarsely granular and brownish yellow. The right lobe was smaller than the left, the right lobe measuring

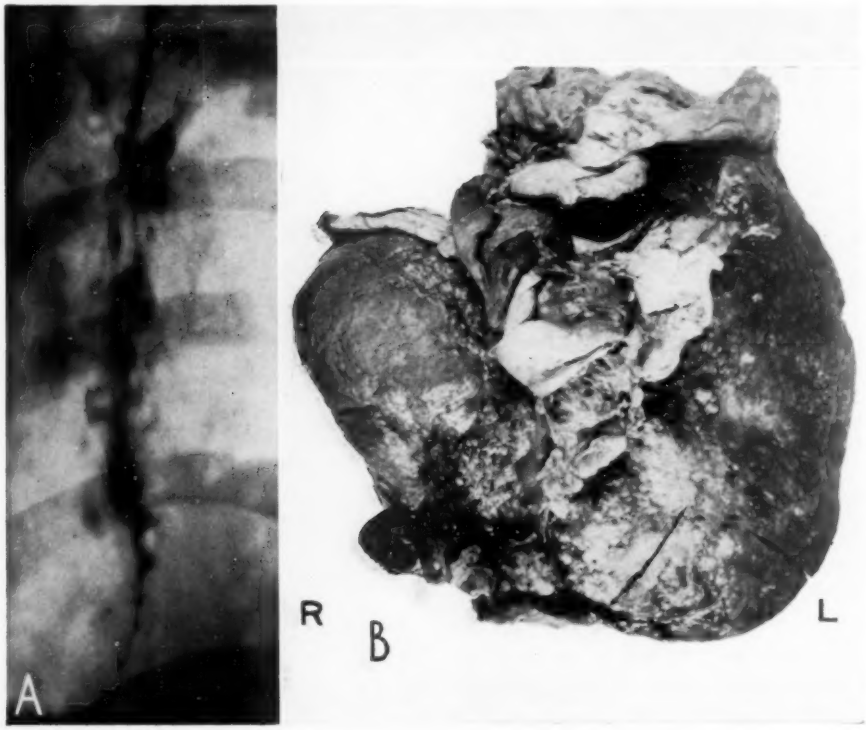

Fig. 2. Case 1. *A*, roentgenogram of the lower half of the esophagus showing extensive varicosities. *B*, anterior view of the liver at autopsy. Tumor mass in the left lobe of the liver. Compare the large left lobe and the small right lobe with the findings at the gastrointestinal examination (see Fig. 1, *B*).

15×15×9 cm., the left lobe 30×20 cm. On its anterior surface the left lobe showed an area measuring about 12 cm. in diameter which on section showed irregular infiltration with white, grayish tissue. The entire left lobe had flecks of this grayish material in its cut surface. They were also present in the right lobe but not so marked. There was a neoplastic thrombus in the hepatic vein. Metastases were found in the glands around the pancreas and in the lungs, the metastases being primarily blood borne with secondary lymphatic extension.

Histological examination of the tumor tissue showed characteristic hepatoma (large acidophilic cells with prominent cell membranes, vaculated cytoplasm, up to 10–15 nuclei in a single cell). The anatomical diagnosis was that of toxic cirrhosis of the liver, primary liver cell carcinoma (hepatoma) with metastases to the lungs and the retroperitoneal lymph glands.

Comment. The diagnosis in this case was not based on a single roentgenological sign, but rather on a combination of several signs. This man had a mass which was extrinsic to the stomach, apparently in the left lobe of the liver or close to it. The metastases in the chest confirmed the impression that the mass represented a malignant tumor. The demonstration of varices within the esophagus indicated an obstruction in the portal system, presumably due to cirrhosis of the liver. This assumption was supported by the fact that the right lobe of the liver appeared to be small. Realizing the common association of cirrhosis with primary cancer of the liver, such a diagnosis seemed to be the only logical explanation of all the findings.

This case prompted us to review the cases of primary cancer of the liver autopsied in the Massachusetts General Hospital within the last thirteen years. In 7 cases, no roentgen examination had been made. In others, only the reports of the roentgen examinations and no films were available. In one of these the right diaphragm was reported to be high in position and to show limited excursion. In another case with ascites, both sides of the diaphragm seemed to be high. The gastrointestinal examination in 3 cases was reported to be negative; in a fourth case extrinsic pressure on the first and second portion of the duodenum was noted.

In one operative case and in 2 autopsy cases the chest findings were of interest (Cases II, III and IV).

Case II (Case Records of the Massachusetts General Hospital; Case 22051)[4] (Fig. 3). An Italian laborer, aged fifty-six, entered the hospital complaining of pain in the mid epigastrium on breathing. This pain had been present more or less severely for the last eight months following a cold. The cough had remained, nonproductive and not very persistent. He had lost about 5–10 pounds during this time. Physical examination was essentially negative with exception of the chest examination which showed diminished breath sounds over the right base with questionable slight increase in fremitus. The abdominal wall was very thick but the tip of the spleen was said to be palpable by one examiner only. The blood picture was that of macrocytic anemia.

Roentgen examination showed a sharply defined mass in the region of the right diaphragm which on the lateral view was seen to lie in the anterior part of the chest. It was about 10 cm. wide, 11 cm. deep and arose about 4 cm. above the posterior part of the right diaphragm. There were linear markings of increased density in the right middle lobe probably due to poor aeration. The examiner thought the mass to be above the right diaphragm. Lipiodol examination and pneumothorax proved the mass to be outside the lung and to be inseparable from the shadow of the diaphragm which showed limited motion. No gastrointestinal examination was done.

A transpleural exploration was performed by Dr. Edward D. Churchill. It became immediately apparent that the mass lay beneath the diaphragm. After incision of the diaphragm a tumor mass apparently arising from the liver was exposed and a biopsy was taken. The liver itself around the tumor was rough and nodular, apparently cirrhotic. The biopsy specimen showed cells similar to liver cells in appearance but rapidly growing, atypical and evidently neoplastic. Here and there they surrounded small canaliculi, and there were masses of inspissated bile; in other words, a typical hepatoma was present (Dr. Tracy B. Mallory).

Comment. A large primary cancer of the liver had produced a localized elevation of

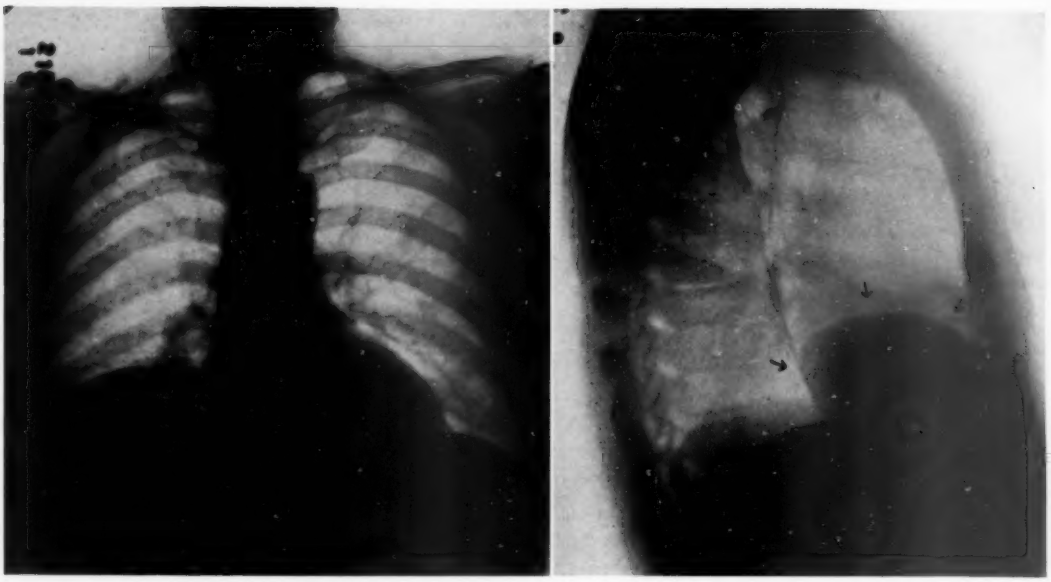

Fig. 3. Case II. Localized elevation of the anterior portion of the right diaphragm produced by a hepatoma.

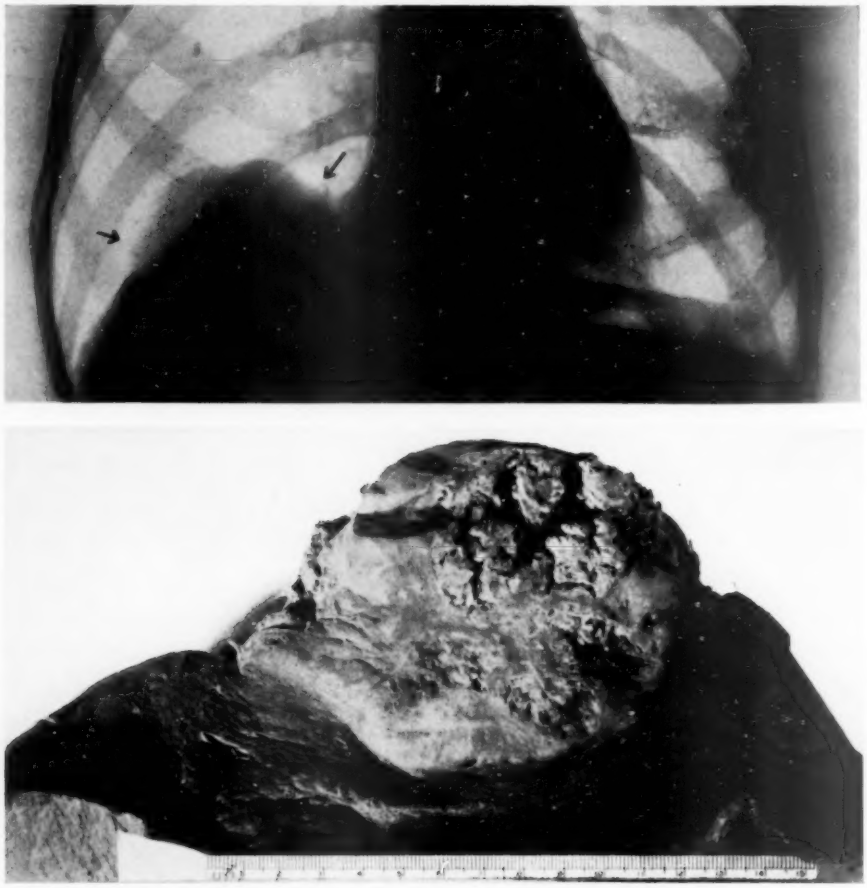

Fig. 4. Case III. Localized bulge of the dome of the right diaphragm produced by a localized cholangioma (calcification of the left pleura is present as an accidental finding).

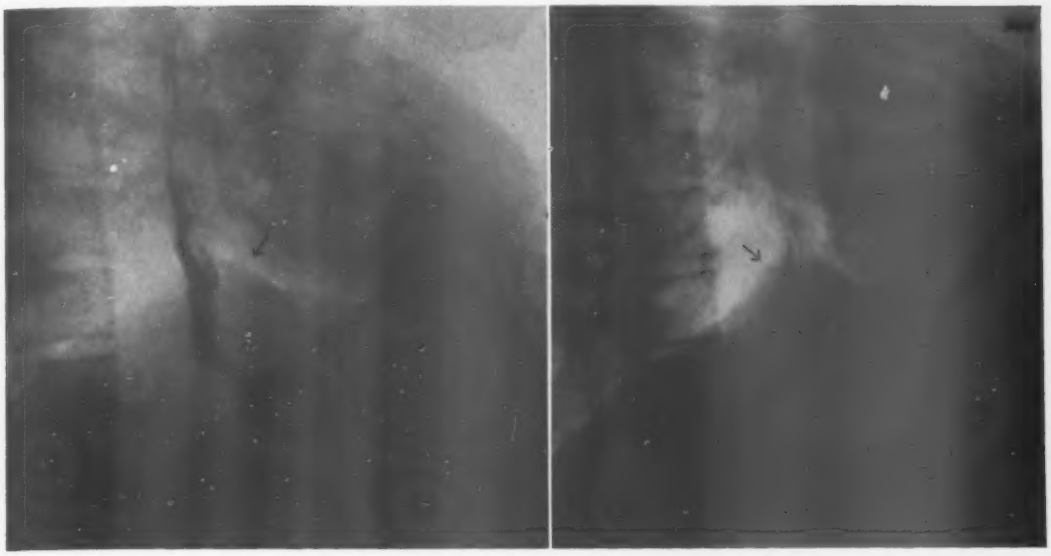

FIG. 5. Case IV. Varices of the lower end of the esophagus and localized bulge of the right diaphragm in a patient with hepatoma.

the right diaphragm. No gastrointestinal examination was made, and the question whether or not varices were present remains unanswered.

CASE III (Case Records of the Massachusetts General Hospital; Case 20011)[6] (Fig. 4). A man, aged seventy, entered the Out Patient Department complaining of shortness of breath for the last four months. He had lost 30 pounds in weight during the past year. Physical examination showed an emaciated patient. There was a palpable mass in the right epigastric region. It measured approximately 10 cm. in diameter and moved with respiration. A roentgenogram of the chest showed evidence of old apical tuberculosis, extensive calcification of the pleura on the left side as well as a bulge in the mid portion of the right diaphragm measuring about 8.5 cm. in width and about 2.5 cm. in height. No lateral film was taken. Examination of the gastrointestinal tract was said to be negative. Approximately five months later he was admitted to the hospital because of coma of five days' duration and he died on the fourth day after admission.

At autopsy the liver was found to weigh 1,900 grams. It was a markedly cirrhotic liver due to hemochromatosis. Within the right lobe of the liver there was a single large mass measuring 11×11×6 cm. It protruded over the superior surface of the liver and was in places adherent to the diaphragm. There were metastases to the lymph nodes around the common duct and to the retroperitoneal lymph nodes. No esophageal varices were seen. Histopathological examination proved the presence of hemochromatosis. The tumor itself contained much connective tissue and relatively few tumor cells. The cells had a tendency to be in glandular arrangement. The anatomical diagnosis was hemochromatosis and primary adenocarcinoma of the liver (cholangioma).

Comment. This case is similar to the preceding one, in that there was a localized elevation of the right diaphragm resulting from the tumor mass in the liver.

CASE IV (M. G. H. 224028) (Fig. 5). An Armenian laborer, aged fifty-one, entered the hospital with a history of swelling of the abdomen for a period of three weeks. He had been a moderately heavy drinker for the last thirty-five years. Three months ago he noticed that his abdomen became distended, and this progressed steadily until the time of his admission to the hospital. Otherwise he felt well. Physical examination showed a distended abdomen with fluid waves. Liver and spleen could not be felt on account of the distention.

Roentgen examination of the esophagus showed irregularities of the lower third which were thought to be consistent with varices. The films showed in addition a small bulge in the mid portion of the right diaphragm which was

not described in the report. A diagnosis of cirrhosis of the liver was made. The patient was discharged. After repeated ambulatory abdominal taps he entered the hospital again four months after the first admission in a comatose condition and died five days after admission. No roentgenological studies were done at the second admission.

At autopsy a large protruding mass was found in the diaphragmatic aspect of the right lobe of the liver. The rest of the liver showed evidence of cirrhosis. Histopathological examination showed the presence of primary liver cell carcinoma (hepatoma).

Comment. In this case, esophageal varices were visible as evidence of cirrhosis of the liver. In addition there was a localized lobulation of the right diaphragm which later was found to correspond to a protruding tumor mass on the liver surface.

DISCUSSION

The roentgenological diagnosis of primary cancer of the liver is based on the fact that it is usually associated with cirrhosis of the liver (in 87 per cent of the cases autopsied at the Massachusetts General Hospital). A correct diagnosis is rarely possible until the diagnosis of cirrhosis has been made. The presence of cirrhosis must be demonstrated first. Roentgenologically one may see a large spleen and at times an unusually small liver shadow. Of much greater importance is the demonstration of varices in the esophagus. Varices involving the lower end of the esophagus indicate obstruction in the portal system, and in an adult only cirrhosis of the liver or thrombosis of the splenic vein has to be considered as a causative factor. Varices are not seen in all cases of liver cirrhosis. In a former paper I[19] have shown that they are demonstrable in approximately 50 per cent of the cases. In a large series of cases with esophageal varices we have not seen one proved case in which compression of the portal vein by tumor tissue was the cause of demonstrable varices. This experience is supported by that of the pathologist (Mallory[17]).

In addition to the diagnosis of cirrhosis of the liver a demonstration of a mass in the region of the liver is necessary. This mass may at times be seen on a good roentgenogram of the abdomen. At other times, it may be visualized by the displacement of the stomach, duodenum, colon and occasionally the small intestine. At autopsy the tumor masses are often seen protruding from the surface of the liver. They may result in the formation of a localized bulge in the diaphragm, usually on the right side. The resulting picture is by no means pathognomonic, especially if the bulge is present in the anterior portion of the diaphragm. The appearance of the diaphragm may simulate closely the picture so commonly produced by variations in the development of different parts of the diaphragmatic muscle.

Aside from the two causes just mentioned, lobulation of the diaphragmatic shadow may be produced by other intrahepatic lesions such as metastatic tumors, echinococcus cysts and possibly gumma. It seems, however, justifiable to state that in a patient with proved cirrhosis of the liver any localized bulge of the diaphragm should be taken more seriously than usual, particularly if it occurs in an unusual location, and in all such cases the possibility of a primary cancer of the liver should be considered. The rapid growth which is found in the majority of cases of primary carcinoma of the liver may result in significant rapid changes in the bulge of the diaphragm or in the size of the liver as a whole.

A combination of cirrhosis of the liver (varices) and a mass in the region of the liver is very suggestive of a primary cancer of the liver. The combination of cirrhosis (varices) and positive evidence of cancer (i.e., lung metastases) is less conclusive. However, a combination of all three factors, namely varices, a mass in the region of the liver and metastasis, such as occurred in Case 1, makes the presence of primary cancer of the liver very likely.

Of course it is not possible to rule out definitely the presence of two independent diseases, for example, cirrhosis of the liver together with carcinoma of the pancreas with metastases to the lung. The likelihood

of the presence of a primary carcinoma of the liver in combination with cirrhosis of the liver is, however, greater than other possibilities, particularly when tumors of the gastrointestinal tract have been ruled out.

The diagnosis of primary carcinoma of the liver may occasionally justify an attempt at surgical removal of the tumor. A few such operations have been reported (see Abel[1]).

SUMMARY

(1) A roentgenological syndrome is presented which is thought to be highly suggestive of primary carcinoma of the liver. It is based on the fact that in the large majority of cases this tumor is associated with cirrhosis of the liver.

(2) The syndrome consists in the demonstration of (a) cirrhosis of the liver (esophageal varices, and/or large spleen with small liver); (b) a mass in the region of the liver; (c) positive evidence of cancer (metastasis).

A combination of (a) and (b) alone is suggestive evidence of primary carcinoma of the liver; a combination of (a) and (c) alone is much less conclusive.

A purely roentgenological diagnosis is not possible in those cases in which cirrhosis of the liver is not present or cannot be demonstrated roentgenologically.

(3) A localized bulge in the diaphragm, a not uncommon normal finding, should be considered more seriously if it occurs in a case with cirrhosis of the liver.*

REFERENCES

1. Abel, A. L. Primary carcinoma of the liver; with report of a case successfully treated by partial hepatectomy. *Brit. J. Surg.*, 1934, *21*, 684–700.
2. Beckermann, F., and Popken, C. Kontrastdarstellung der Leber und Milz im Röntgenbild mit Jodsolen. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1938, *58*, 519–535.
3. Boyce, F. F., and McFetridge, E. M. Primary carcinoma of the liver, with report of 28 additional cases. *Internat. Surg. Digest*, 1934, *18*, 67–80.
4. Case Records of the Massachusetts General Hospital; Case 22051. *New England J. Med.*, 1936, *214*, 209.
5. Case Records of the Massachusetts General Hospital; Case 23051. *New England J. Med.*, 1937, *216*, 209.
6. Case Records of the Massachusetts General Hospital; Case 20011. *New England J. Med.*, 1934, *210*, 36.
7. Charache, H. Primary carcinoma of the liver; report of case and review of literature. *Am. J. Surg.*, 1939, *43*, 96–105.
8. Eggel, H. Ueber das primäre Carcinom der Leber. *Beitr. z. path. Anat. u. z. allg. Path.*, 1901, *30*, 506–604.
9. Ehrlich, D. E., and Ansanelli, F. C. Primary carcinoma of liver with hepatosplenography. *J. Am. M. Ass.*, 1935, *105*, 355–356.
10. Ewing, J. Neoplastic Diseases. Third edition. W. B. Saunders Co., Philadelphia, 1931.
11. Greene, J. M. Primary carcinoma of the liver: ten-year collective review. *Internat. Abstr. Surg.*, 1939, *69*, 231–236. In *Surg., Gynec. & Obst.*, 1939, *69*.
12. Gregory, R. Primary carcinoma of the liver; tumor thrombosis of inferior vena cava and right auricle. *Arch. Int. Med.*, 1939, *64*, 566–578.
13. Gustafson, E. G. Analysis of 62 cases of primary carcinoma of the liver based on 24,400 necropsies at Bellevue Hospital. *Ann. Int. Med.*, 1937, *11*, 889–900.
14. Jaffe, R. H. Quoted from Greene, ref. 11.
15. Liber, A. F., and Brown, C. R. Primary liver cell carcinoma with splenic metastases. *Am. J. Cancer*, 1939, *35*, 521–527.
16. Loesch, J. Primary carcinoma of the liver. *Arch. Path.*, 1939, *28*, 223–235.
17. Mallory, T. B. *New England J. Med.*, 1937, *216*, 211.
18. Novati, G. C. Contributo radiologico alla diagnosi di tumore primitivo del fegato. *Radiol. med.*, 1936, *17*, 21–26. Abstr. Am. J. Roentgenol. & Rad. Therapy, 1937, *37*, 561.
19. Schatzki, R. Roentgen demonstration of esophageal varices; its clinical importance. *Arch. Surg.*, 1940, *41*, 1084–1100.
20. Schnabel, T. G. Primary carcinoma of the liver with spontaneous rupture and lethal hemorrhage. *Ann. Surg.*, 1935, *101*, 613–616.
21. Steiner, M. M. Primary carcinoma of the liver in childhood. *Am. J. Dis. Child.*, 1938, *55*, 807–824.
22. Strong, G. F., and Pitts, H. H. Primary carcinoma of the liver. *Arch. Int. Med.*, 1930, *46*, 105–120.

* Since this report was written 2 additional cases of hepatoma were examined in the Roentgenological Department of the Massachusetts General Hospital, one of them being proved by autopsy, the other by biopsy. In both cases, varices of the esophagus as well as a localized bulge of the diaphragm, corresponding to the tumor mass, were seen roentgenologically.

AN UNUSUAL INTRACRANIAL FOREIGN BODY*†

By ROBERT DRANE, M.D.
SAVANNAH, GEORGIA

G. K., white, male, aged sixteen, on March 12, 1935, at four-thirty in the afternoon, was struck in the left eye with the tip of his opponent's foil while fencing without a mask. He dropped to the floor, but quickly regained his composure and equilibrium, and walked three blocks to an ophthalmologist's office. The following diagnosis was made: "Abrasion of cornea with small triangular flap torn loose at seven o'clock—laceration of the conjunctiva." There was some proptosis present. The left pupil was irregularly dilated and fixed. The ophthalmoscope showed no hemorrhage and no detachment of the retina. There was limitation of movement in all directions. The injury was not considered serious.

He was sent to the hospital for observation and treatment of his eye. He was pale and in very slight shock.

Next morning there was increased proptosis, edema, and ecchymosis of the lids. The patient complained of increasing headache and drowsiness, and he was irritable. His temperature was 102.2° F.; white blood count 14,600, with 89 per cent polymorphonuclears. The stupor increased and more significance was placed upon the accident.

On the afternoon following the accident, it was discovered that the tip of the foil in question was missing. A search of the room failed to locate it. When this was learned at the hospital, it was thought advisable to make roentgenograms of the orbit. To the consternation of all, the tip was seen in the region of the left posterior lobe.

I was called to the hospital and, under roentgenoscopic localization, designated its near point.

At operation, 1:05 A.M., approximately thirty-two hours after the injury, the dura was found injured. It was opened; clotted blood and brain tissue escaped under pressure. The foreign body was easily located, 1 cm. beneath the dura, and withdrawn. The wound was irrigated with saline through a catheter. The dura was not closed on account of the pressure, and the skull flap was removed. The scalp was closed without drainage and a snug bandage applied.

A spinal puncture just after the operation showed the pressure to be 10 mm. and the fluid cloudy. It contained red blood cells and no pus cells. Bacterial culture was not reported.

On March 15, the temperature was 101.2° F., blood pressure, 136/56; pulse, 92. The patient was incoherent. However, the temperature and mental condition became normal within six days. The wound healed without infection and with only slight bulging.

Following the operation, there was some edema of the retina of the left eye. This gradually cleared up by the fourth day when he could count fingers.

On March 21, the following report was made: "Eye quiet; good motion up and down; some limitation on internal rotation; no outward rotation."

On March 22: "Slight internal squint due to weakening of the external rectus—pressure from hemorrhage (?)."

On March 29: "Pupil contracting nicely; fundus normal; slight internal squint."

There was no demonstrable damage other than the slight squint.

Examination in August, 1940, showed no bulging of the scalp; no impairment in the vision or muscular movements; no disturbance in the sensory or motor functions; and no mental disturbance.*†

* This case is reported through the courtesy of Drs. Craig Barrow and M. J. Egan of Savannah, Ga.

† For discussion see page 495.

* This case is reported as a medical curiosity. The fortunate outcome precludes an accurate description of the tract of the foil.

† Read at the Forty-first Annual Meeting, American Roentgen Ray Society, Boston, Mass., Oct. 1–4, 1940.

NEUROBLASTOMA SYMPATHETICUM

ROENTGENOLOGICAL APPEARANCES AND RADIATION TREATMENT*

By GEORGE M. WYATT *and* SIDNEY FARBER
BOSTON, MASSACHUSETTS

THE neuroblastoma is one of the most frequently encountered malignant tumors of infants and children. Forty examples were recorded in a series of 301 malignant tumors, verified histologically at the Boston Children's Hospital during the ten year period ending September 1, 1939.[4] During the same period, 30 embryomas of the kidney (Wilms' tumor) were studied. An analysis of those 40 instances of neuroblastoma with particular reference to the bearing on prognosis and treatment of the life history and behavior of the tumor has been reported recently by one of us (S.F.[5]). Roentgenologic studies were made on 34 of those 40 patients. It is the purpose of this communication to describe the roentgenological manifestations of the neuroblastomas as observed in this series, and to document in greater detail certain conclusions previously reported from this hospital concerning the rôle of irradiation in the treatment of the neuroblastoma.[5]

The conclusion derived from Farber's[5] analysis of the 40 instances of the neuroblastoma may be summarized briefly. The term neuroblastoma or sympathetic neuroblastoma was used to denote the malignant member of the series of tumors arising in the sympathetic nervous system. The primary tumor arose not only in the adrenal medulla but also in many other situations in the body, such as ganglions, adjacent to the adrenal gland, the celiac plexus, the organ of Zuckerkandl near the bifurcation of the iliac arteries, the cervical ganglions, and ganglions in various retroperitoneal and retropleural locations with extension into the extradural space surrounding the spinal cord. No support was obtained for the perpetuation of designations such as Pepper's or Hutchinson's type of neuroblastoma. At the time of that report, 10 of the 40 patients studied were alive from three to eight years after operative discovery and histologic verification of the nature of the tumor, an experience at variance with the almost hopeless prognosis recorded in the literature.[1,10] Farber made three observations concerning the life history and treatment of the neuroblastoma on the basis of his studies: (1) the neuroblastoma may undergo spontaneous hemorrhage and necrosis, and disappear without any treatment; (2) the neuroblastoma may undergo spontaneous maturation and become a benign ganglioneuroma; (3) the neuroblastoma may be treated successfully by a combination of surgical intervention and irradiation even after proved local metastasis, such as to the liver, has occurred.

ROENTGENOLOGICAL FINDINGS

Roentgenological studies were carried out in 34 of the 40 instances of neuroblastoma verified histologically at the Children's Hospital during the ten year period ending September 1, 1939. The ages of the patients ranged from four days to eight years and eleven months, although the majority were under the age of four years. There was considerable variation in the nature of the complaints for which the patients were referred to the roentgen department. The presence of an abdominal mass was mentioned most frequently, after which abdominal pain with or without abdominal mass, pain in the back or in the extremities because of metastases, and a long series of less specific complaints, such as fever, anorexia, jaundice, hematemesis, diarrhea, constipation, and loss of weight may be listed. The roentgenological find-

* From the Departments of Roentgenology and Pathology of the Children's Hospital, and the Department of Pathology of Harvard Medical School, Boston. Read at the Forty-first Annual Meeting, American Roentgen Ray Society, Boston, Mass., Oct. 1–4, 1940.

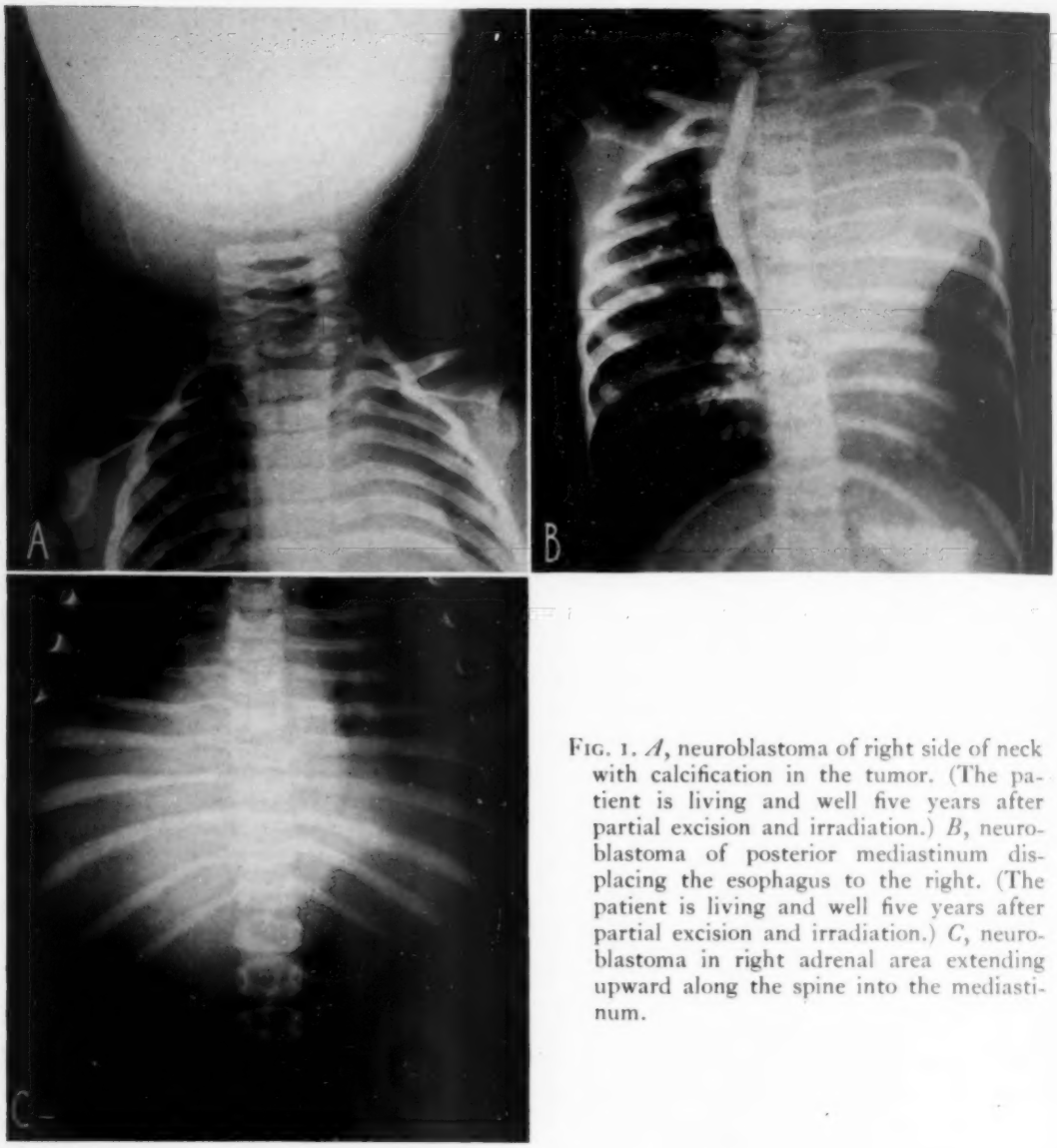

Fig. 1. *A*, neuroblastoma of right side of neck with calcification in the tumor. (The patient is living and well five years after partial excision and irradiation.) *B*, neuroblastoma of posterior mediastinum displacing the esophagus to the right. (The patient is living and well five years after partial excision and irradiation.) *C*, neuroblastoma in right adrenal area extending upward along the spine into the mediastinum.

ings will be considered in relation to (1) the location and appearance of the primary tumor, and (2) the location and character of the metastases.

PRIMARY TUMOR

In 7 of the 34 patients no primary tumor was demonstrable roentgenologically although all 7 patients had metastases at the time of examination. It should be mentioned that complete utilization of special diagnostic procedures was not possible in all cases because of the illness of the patient. In one instance, however, the use of every available approach failed to reveal a primary tumor in a patient who later developed a very large abdominal mass.

Most of the tumors which were demonstrable roentgenologically were located in the abdomen (17 instances), and always in the posterior portion of the abdominal cavity. The posterior mediastinum was the next most frequent site of the primary tumor (Fig. 1, *B*). The remainder arose from the sympathetic chain anywhere from the cervical region (Fig. 1, *A*) to the pelvis.

Two tumors in this series were located in the lower dorsal and upper spinal canal.

A rough classification which permitted a comparison of the size of the tumor to the size of the patient was made on the basis of displacement of adjacent structures. Gross displacement was noted in 23 of 27 patients in whom a primary tumor could be identified roentgenologically. The amount of displacement varied from that which was barely demonstrable to severe distortion occasioned by tumors which filled almost the entire abdominal cavity.

Calcium deposits in the tumors were present in 6 instances (Fig. 1, *A*). The appearance of this calcification varied from fine uniform stippling in the center of the tumor to irregular confluent shadows of increased density throughout the tumor mass.

Pyelograms were obtained on 6 of the patients with demonstrable abdominal masses. In 5 of these 6 patients the homolateral kidney was displaced downward and laterally, and in the remaining instance there was forward displacement of both ureters with partial ureteral obstruction, but no demonstrable displacement of the kidney. It would be expected, of course, that a tumor arising in the adrenal gland would cause, in most instances, lateral and downward displacement of the kidney. Such a characteristic, however, is not peculiar to the neuroblastoma, since a similar situation may be brought about by an embryoma arising in the upper and medial aspect of the kidney. The roentgenological picture produced by neuroblastoma arising in the adrenal may be confused, not only with the embryoma of the kidney, but also with hydronephrosis, mesenteric cyst, massive unattached retroperitoneal embryoma, massive hemorrhage into the adrenal gland, particularly in the neonatal period, to mention only the more common conditions in that region. Similar confusing possibilities in the many other locations in the body from which neuroblastoma may arise preclude the formulation of any characteristic roentgenological picture. A definite diagnosis of primary neuroblastoma can be made only on the basis of histologic study of tumor tissue.

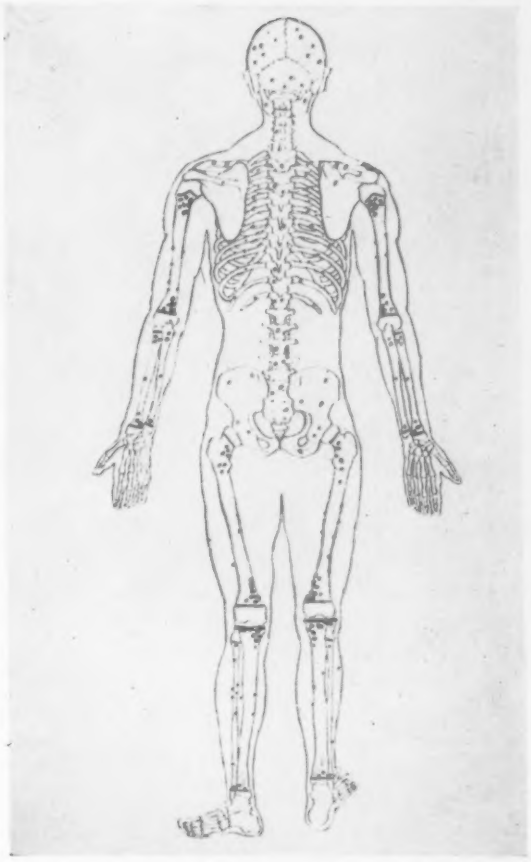

Fig. 2. Composite diagram illustrating the location and distribution of skeletal metastases in 15 patients of this series.

METASTASES

To Soft Tissues. Most of the metastases to soft tissue occurred in the orbits and in the meninges. Five of the patients had metastases to the orbits, as was shown by exophthalmos, hemorrhage, and tumor infiltration into the retro-orbital tissues. Destruction of the orbital bones was demonstrable in most of these patients, and palpable masses in the scalp were accompanied invariably by underlying lesions in the cranial vault. Separation of the cranial sutures secondary to increased intracranial pressure occasioned by metastases to the meninges was observed in 6 instances (Fig.

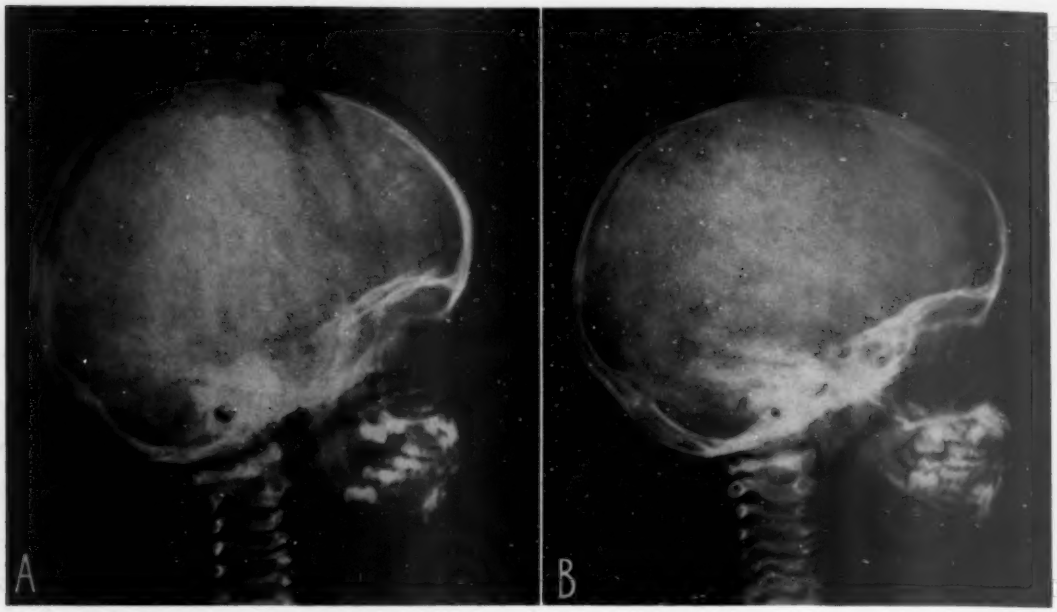

Fig. 3. *A*, widespread miliary metastases with bone proliferation in the cranial vault and separation of the coronal suture. This was the usual appearance of skull metastases. *B*, relatively large osteolytic metastases in the parietal bone. This type of skull metastasis was seen in only one case.

3, *A*). Mediastinal masses were demonstrable in 4 instances of large abdominal tumor, 2 of which showed evidence of direct extension through the diaphragm from the abdominal tumor (Fig. 1, *C*). Thickening of the pleura was noted in 4 patients, 3 of whom had metastases also to the ribs. Fluid in the pleural cavity was present in 2 instances. In only a few patients were metastases in the long bones accompanied by masses in the adjacent soft tissue.

Fig. 4. Metastases in the pelvic bones showing mainly proliferation with some bone destruction. This type of change was seen most frequently in the pelvis and spine.

To Bone. In 15 of the 34 patients metastases to the skeleton were demonstrated roentgenologically. These were found in every part of the skeletal system with the exception of the metacarpal and metatarsal bones, and phalanges (Fig. 2). Three or more portions of the skeleton were involved in all but two instances. The majority of the patients had generalized metastases to all bones proximal to the knee and elbow joints. In 4 patients lesions were present also in places distal to these joints. Epiphyseal involvement was rare.

One striking feature in the distribution of bone metastases was the frequency of bilaterally symmetrical lesions. Bilateral involvement of one or more parts of the skeletal system was present in all but one of the 15 patients. The sites most frequently involved by the symmetrically placed metastases were the diaphyseal portions of the humerus, the distal portion of the femur,

and the pelvis, although such lesions occurred also in the clavicle, tibia, and other bones.

The metastases to bone varied in character from those showing only destruction of bone to those which gave a picture of both endosteal destruction and proliferation, and those showing chiefly proliferation of the periosteum. Metastases which produced massive destruction were found in 5 patients, occurring in most instances at the ends of diaphyses, immediately beneath the metaphyseal margins (Fig. 5, *B*). Pathological fractures, when present, occurred through lesions of this type. Combined bone destruction and proliferation was present in the majority of lesions, the most common form being characterized by the presence of multiple small discrete and confluent areas of destruction with a small amount of proliferation of the surrounding bone. Proliferation was a prominent feature in the spine and pelvis (Fig. 4), in some instances simulating Paget's disease; the lesions in the skull (Fig. 3, *A* and *B*), ribs, and shafts of the long bones were predominantly destructive in type. Proliferation of the periosteum overlying metastases to the shaft of the long bones occurred in 6 patients.[2] Elevation of the periosteum was noted in one instance before involvement of the subjacent bone was demonstrable. Illustrations of different stages of periosteal reaction are shown in Figure 7, *A* and *B*. No instance of the commonly described spicule formation at right angles to the shaft was found in this series.[7,8,11] It was interesting to note that not only did the periosteal reactions stop short of the ends of the diaphyses, but that such reaction was entirely lacking in the presence of gross destruction in the submetaphyseal areas (Fig. 6, *A* and *B*).

Fig. 5. *A*, bilaterally symmetrical areas of miliary and confluent bone destruction with slight proliferation in the proximal diaphyseal ends of both humeri. This was the most common type of metastases to the long bones. *B*, bilaterally symmetrical destructive lesions in the distal portions of the femoral diaphyses. This type of massive bone destruction occurred usually at the diaphyseal ends and was responsible for most of the pathological fractures which occurred in this series.

Bone metastases in general were all of

Fig. 6. *A*, metastases with massive bone destruction in the distal portions of the right radius and ulna. There is also a metastasis with a pathological fracture in the proximal portion of the left radius and lesions with fracture dislocations of the heads of the humeri. *B*, single osteolytic metastasis in the distal end of the left femur. (One other metastasis was present in the 5th left rib.) This is the only patient with bone metastases in whom no bilaterally symmetrical lesions were found.

similar type in a given case. In no instance was a large destructive lesion in one bone accompanied by predominantly proliferative changes in another bone. Difficulty was encountered sometimes in differentiating between metastases of a neuroblastoma and the involvement of bone caused by tumors of the blood-forming tissues, such as leukemia. In some instances the appearance was practically identical (Fig. 8, *A*). In others, the problem of differential diagnosis was simplified by the finding of leukemic infiltration in the bones of the hands and feet (Fig. 8, *B*), a site of involvement we have never encountered in patients with neuroblastoma. Careful hematologic study will reveal the presence of leukemia in most instances. A tentative diagnosis of neuroblastoma was made in all but two instances when metastases to the skeleton were present. The generalization should be made that roentgenological examination of the chest and of the entire skeleton should be instituted whenever a solid tumor mass is found in an infant or child.

Fig. 7. *A*, thin line of raised subperiosteal new bone secondary to metastasis in the femur. *B*, same area three months later showing subperiosteal new bone broken sharply at its distal margin.

RADIATION THERAPY

With one exception,[5] reports in the literature concerning the use of irradiation in the

treatment of neuroblastoma indicate that permanent cures have not been obtained, although temporary improvement has been observed.[2,6,8] In most of the patients described in the literature, metastases were widespread when the patients were first seen. In the earlier reports massive doses were employed. The possibility of achieving better results in the treatment of neuroblastoma by the use of small divided doses was first mentioned by Hauser[6] in 1934.

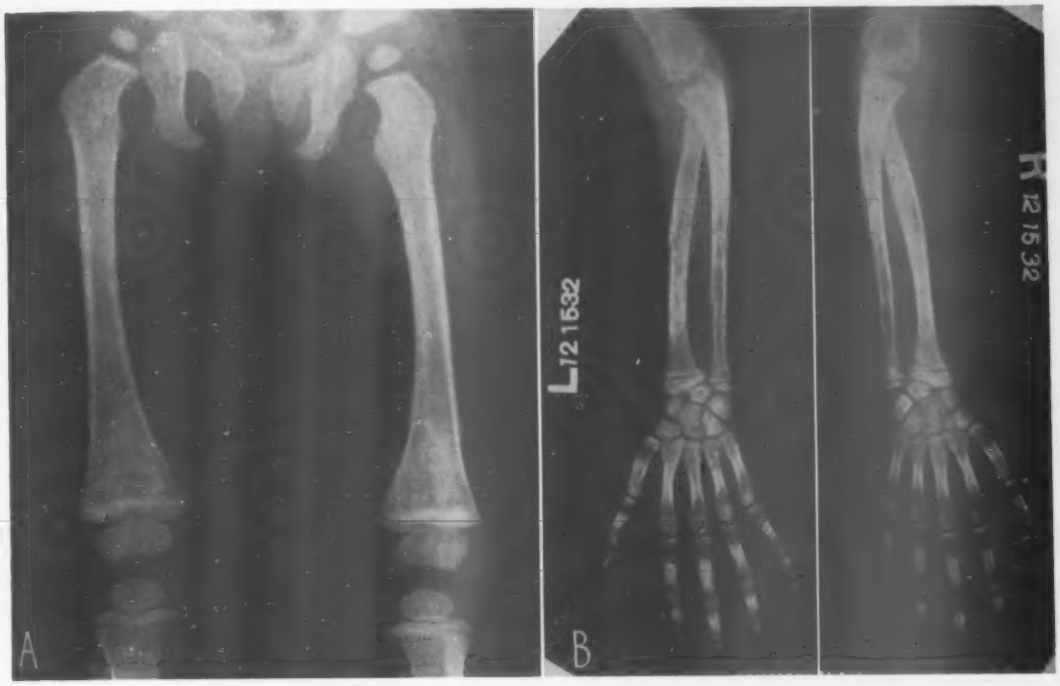

FIG. 8. *A*, subperiosteal new bone with broken distal margins seen in a patient with a tumor of the blood forming tissues (hematocytoblastoma), simulating the appearance seen in neuroblastoma. *B*, bone destruction in a case of advanced myeloid leukemia, with lesions of the metacarpal bones and phalanges in addition to those in the radius and ulna. Metastases from neuroblastoma were never seen distal to the wrist and ankle joint.

Any evaluation of irradiation in the treatment of the neuroblastoma must take into consideration the usual survival period and the circumstances surrounding, if not responsible for, the reported cures. Blacklock found that the average length of life of patients with adrenal neuroblastoma from the time of onset of clinical symptoms until death was between eight and nine weeks. Death occurred in every case.[1] Redman and his coworkers, in a comprehensive review of reported cases of neuroblastoma, observed that the outcome was almost invariably fatal within a few months after the onset of symptoms.[10] Among the small number of cures there may be cited the remarkable experience of Cushing and Wolbach,[3] who observed the maturation of a malignant neuroblastoma into a benign ganglioneuroma. Lehman[9] reported a twenty year survival after simple excision of the primary tumor.

According to Farber's[5] analysis, the 10 patients who survived in the Children's Hospital series of 40 instances of neuroblastoma received treatment which varied as follows:

A. Without irradiation:

1. Biopsy of an inoperable tumor which had not metastasized.

2. Complete surgical removal of a primary tumor without evidence of metastasis.
3. Incomplete removal of a primary tumor which was undergoing differentiation into a ganglioneuroma.

B. With irradiation:

1. Complete surgical removal of a primary tumor without evidence of metastases.
2. Complete surgical removal of a primary tumor and biopsy of one of numerous metastases to the liver.
3. Biopsy of a metastasis of a primary neuroblastoma to the liver without removal of the primary mass.
4. Incomplete removal of a primary tumor which was undergoing differentiation into a ganglioneuroma.

Ten of the patients in Farber's series received radiation therapy. Five of these are still living and without evidence of disease, two to five years after treatment,* even though known local metastases were present in 2 instances at the time therapy was instituted. Of the 5 patients who received radiation therapy and died, 3 had extensive metastases to the skeleton when first observed. Two patients had only local metastases when first seen, but developed bone lesions while receiving local irradiation.

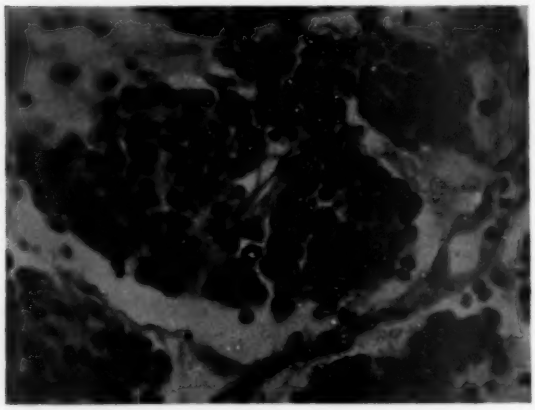

Fig. 9. Photomicrograph of liver metastasis in Case II. Patient is living and without evidence of disease two years after radiation treatment. Note typical pseudorosettes surrounding pale fibrils representative of axis cylinder processes.

* Two of these patients were treated by Dr. M. C. Sosman, to whom acknowledgment is made also for the use of data concerning radiation therapy in Case I.

In 1940, Farber reported the cure for the first time of a patient with neuroblastoma after the liver had been involved by multiple metastatic nodules (Case I below).[5] To this experience we should like to add a similar one (Case II), with the pertinent details of therapy.

Case I. R. C., a female baby, aged eleven days, was subjected to laparotomy because of a large mass in the right flank and an enlarged liver. Despite the fact that multiple metastases were present in the liver, a primary tumor of the right adrenal was removed as was a biopsy of one of the many nodules in the liver. The patient was referred to Dr. Merrill C. Sosman of the Peter Bent Brigham Hospital for radiation therapy, which was instituted two weeks after operation. Two courses of treatments were given to the abdomen through two 15×15 cm. portals, anterior and posterior fields being treated on alternate days. (Factors: 200 kv., 18 ma., 2.0 mm. Cu+1.0 mm. Al filtration, 50 cm. target-skin distance, 105 r, measured in air.) The first course consisted of 1,570 r, given over a period of fifteen days. The second course was started two months later, but was discontinued because of leukopenia after 672 r had been administered.

The patient is now alive and in excellent health somewhat over three years after treatment. The liver is normal in size and there is no evidence of metastases elsewhere in the body.

Case II. A. B., a female baby, aged three months, was explored surgically because of hepatomegaly of unknown etiology (Fig. 10, *A*). A biopsy was taken from one of numerous nodules on the surface of the enlarged liver. The pathologic diagnosis was neuroblastoma (Fig. 9), metastatic to the liver. No search was made for the primary tumor because of the poor condition of the patient.

The liver continued to increase rapidly in size following operation. Radiation therapy was instituted at the Children's Hospital by one of us (G.M.W.) on the ninth postoperative day. Daily treatments were given to the abdomen through four 15×12 cm. portals, anterior, pos-

Fig. 10. *A*, huge shadow caused by multiple metastases to liver. Biopsy of a metastatic nodule in the liver was followed by irradiation (Case 11). *B*, same patient four months after roentgen treatment. This patient is still living and well two years following treatment.

terior, right lateral and left lateral fields being treated on successive days. (Factors: 160 kv., 6 ma., 0.5 mm. Cu+1.0 mm. Al filtration, 50 cm. target-skin distance, 75 r in air at the first treatment and 100 r on subsequent days.) A total of 1,575 r was given over a period of three weeks, at the end of which time treatment was discontinued because of the patient's poor general condition and progressive loss of weight.

The liver became smaller during treatment, and continued to decrease in size thereafter until it was no longer palpable although still slightly enlarged (Fig. 10, *B*). This patient is now alive and well two years after treatment.

Caution seems indicated in the treatment of these patients if the immediate result of therapy is not to defeat its ultimate purpose. Grave reactions, for example, followed initial doses of 100 r in some patients who had large abdominal tumors. Rapid shrinkage of many of these tumors led to the conclusion that even a small amount of radiation could produce enough necrosis of the tumor to cause clinical symptoms. The reactions could be explained only partially on the basis of the necessarily large fields which in many instances included the liver. For this reason, it seemed wiser to give an initial test dose of 75 to 100 r, and to increase the subsequent doses with the severity of reaction as a guide. Frequent blood counts were made to determine the presence of radiation leukopenia. Larger total doses might have been desirable, but were not given because of the unfavorable response of these patients to large amounts of radiation.

None of the patients with widespread metastases was cured by irradiation although remarkable improvement was observed following treatment of 2 such patients (Fig. 11, *A* and *B*). Irradiation of

Fig. 11. *A*, metastases to distal end of femora and proximal end of tibiae producing moth-eaten bone destruction. Note pathological fractures in the distal ends of the femora. *B*, same case showing healing after general body irradiation. This patient died later with recurrence of a large abdominal tumor.

the entire body was employed in these instances because it was probable that widespread metastases were present even though only a few metastases to bone could be demonstrated. More frequent hematologic studies were performed on these patients than in others of this series, since the occurrence of leukopenia is an important danger signal in this type of radiation treatment. Despite the fact that no cures were obtained when irradiation was employed after widespread metastases had occurred, the response was such as to provide encouragement for further efforts in this direction. The alternative of certain death after widespread metastases have occurred is reason enough for the continuation of efforts in treatment.

From this limited experience with the neuroblastoma we conclude that surgical removal of the primary tumor should be the first step in treatment. Should complete excision be impossible, tissue should be removed for histologic study. In every instance, surgical intervention should be followed by irradiation, even when distant metastases are present.

CONCLUSIONS

1. There is no characteristic roentgenological picture of the primary neuroblastoma. A definite diagnosis can be made only by histologic study of tumor tissue.

2. Roentgenologic examination of the entire body is indicated whenever a solid mass is found in an infant or child.

3. When bilaterally symmetrical metastases to bone are present a tentative diagnosis of neuroblastoma may be made in most instances.

4. Radiation therapy should be instituted in every case after the diagnosis has been made.

5. The prognosis even after local metas-

tases have occurred is not hopeless. Radiation treatment should be tried even when metastases to bone are present.

6. Caution is indicated in the amount of radiation used since large amounts are not tolerated well by these patients.

REFERENCES

1. Blacklock, J. W. S. Neurogenic tumours of sympathetic system in children. *J. Path. & Bact.*, 1934, *39*, 27–48.
2. Doub, H. P. Roentgen aspect of sympathetic neuroblastoma. *J. Am. M. Ass.*, 1937, *109*, 1188–1191.
3. Cushing, H., and Wolbach, S. B. Transformation of a malignant paravertebral sympathicoblastoma into a benign ganglioneuroma. *Am. J. Path.*, 1927, *3*, 203–216.
4. Farber, S. Incidence of malignant tumors in infants and children. To be published.
5. Farber, S. Neuroblastoma. Abst. in *Am. J. Dis. Child.*, 1940, *60*, 749–751.
6. Hauser, H. Radiosensitive neuroblastoma. Am. J. Roentgenol. & Rad. Therapy, 1934, *31*, 234–237.
7. Henle, Carye-Belle. Roentgen findings in neuroblastoma. Am. J. Roentgenol. & Rad. Therapy, 1928, *20*, 414–419.
8. Holmes, G. W., and Dresser, R. Roentgenologic observations in neuroblastoma. *J. Am. M. Ass.*, 1928, *91*, 1246–1248.
9. Lehman, E. P. Adrenal neuroblastoma in infancy—fifteen year survival. *Ann. Surg.*, 1932, *95*, 473.
10. Redman, J. L., Agerty, H. A., Barthmaier, O. F., and Fisher, H. R. Adrenal neuroblastoma. *Am. J. Dis. Child.*, 1938, *56*, 1097–1112.
11. Rypins, E. L. Roentgen diagnosis of neuroblastoma in children. Am. J. Roentgenol. & Rad. Therapy, 1937, *37*, 325–332.

DISCUSSION ON PAPERS BY DRS. DRANE AND WYATT AND FARBER

Dr. S. B. Wolbach, Boston. In regard to the paper by Drs. Wyatt and Farber, I am inclined to repeat what Dr. Ernst used to say. For many years he presided over the meeting of the American Association of Pathologists and Bacteriologists, and he used to say that a person who presents a careful study usually knows much more about the subject than those who are asked to discuss it.

What impressed me are, first of all, the cures, and the speculation as to why these spontaneous recoveries occur. Now and then malignant tumors do spontaneously regress, due to factors we know nothing about.

One thing in regard to neuroblastomas which I think will unquestionably be brought out by Dr. Wyatt and Dr. Farber, is that sometimes after exhibiting the microscopic picture of malignancy, they differentiate, become more slowly growing, and reproduce the appearances of so-called ganglioneuromas.

Years ago Dr. Cushing operated on a patient, removing a ganglioneuroma from the back that had apparently emerged from the spinal canal. Years before a tumor had been removed in New York from the same region and called a fibrosarcoma; but when that material was sent down to us, it was easily recognized as a neuroblastoma.

The cure by roentgen irradiation, I think, is a tribute to the very careful work which has been done at the Children's Hospital, and the recognition there that the tumors of early life should be regarded as somewhat different from the tumors of later life, particularly in regard to pathogenesis.

The paper emphasizes, I think, the need of careful study of these tumors and the close cooperation of clinicians, pathologists, and roentgenologists.

One other remark has general application and that is that even in adult life the vagaries of tumors cannot be predicted, and I emphasize, in discussing tumors with my asssociates and with clinicians, that we have no cause ever to be surprised over the behavior of tumors.

I think what Dr. Wyatt has presented should offer a great deal of encouragement.

Dr. J. R. Cooper, New Castle, Pa. During the World War we had a similar case, exactly parallel to this case of Dr. Drane's. This soldier was picked up off a battlefield unconscious and sent to a hospital, but no one ever suspected he had had any real injury to his head. In about two months he was sent back to the Port of New York and was referred to the roentgen department for an examination of his sinuses on account of severe headaches.

The roentgen examination revealed the shadow of a foreign body about the size of a .32 caliber bullet just slightly posterior and below the pineal gland. We then made an intense search for a scar that would indicate a portal of entry of this missile but we were never able to find one. His only complaint was headache. At the time we saw him there was a good sized

area of lesser density about the foreign body indicating a breaking down of the brain structure. No attempt was made to remove the bullet at that time and we were unable to learn the final outcome of the case.

Dr. Ralph S. Bromer, Bryn Mawr, Pa. I feel that I am not qualified to discuss this paper inasmuch as I could only find 6 cases in a comparable ten-year period in the records of the Children's Hospital, Philadelphia, and my experience is limited when compared with that of Dr. Wyatt. However, I wish to emphasize several points which Dr. Wyatt mentioned in his presentation. The first is in regard to treatment, namely, that small initial doses should be given to prevent too rapid dissemination of the tumor and consequent fatal result. The first patient I treated received 200 r through each of two portals and died on the third day following the treatment.

The second point concerns diagnosis. It is most important to examine the entire skeleton, otherwise a single lesion may be diagnosed an osteogenic sarcoma of the osteolytic type. I am again quoting from my own experience. I wish to show a slide of a patient in whom the periosteal changes are more pronounced than in the cases shown by Dr. Wyatt. Earlier writers have stated that periosteal reaction is not prone to occur in neuroblastoma. In the femurs in this patient, the periosteal reaction resembles that shown in the case of Rypins which he called "whisker-like" proliferation. This occurs with sufficient frequency to be regarded as a diagnostic sign.

Dr. Merrill C. Sosman, Boston. I am sure we would like to know how many of these patients remaining cured have had roentgen therapy. Perhaps I should say "apparently cured" instead of "cured."

Dr. Wyatt (closing). In answer to the question by Dr. Sosman, we have considered a one year survival from childhood neuroblastoma equivalent to a five year survival from the average adult cancer. In our series, no recurrences were found among those patients who were symptom free after one year. Most of the patients reported in the literature died within a few weeks following discovery of the disease.

A spontaneous change from malignant neuroblastoma to benign ganglioneuroma did occur in some patients in this series. Any evaluation of roentgen therapy must be considered in the light of those patients who survived without any treatment other than biopsy of the tumor.

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MULTIPLE STRIAE PARALLEL TO EPIPHYSES AND RING SHADOWS AROUND BONE GROWTH CENTERS

By C. A. STAMMEL,* *Lieutenant Colonel, Medical Corps*
UNITED STATES ARMY

THE finding of one or more cross striations in the epiphyseal ends of long bones is not uncommon. By many they are probably wrongfully considered the result of old healed rickets. The presence, however, of many distinct parallel dense lines extending well up into the shafts, together with concentric inclusion ring shadows in the small bones, and many alternating bands of increased and decreased density in the alae of the pelvis, not unlike the growth lines on an oyster shell, is not common. A case presenting this roentgenological appearance was seen at the Station Hospital, Fort Benning, Georgia, in November, 1938. After much consideration and consultation with the available literature and with roentgenological colleagues in the State, I came to the conclusion that I was dealing with an atypical manifestation of the rare Albers-Schönberg's (marble bone) disease. However, in March, 1939, another case showing similar ring shadows and cross striations was encountered. While the roentgen findings in the second case were not quite as striking as in the first case, its appearance caused some doubt to arise regarding the correctness of the first diagnosis. For this reason and because there has been found no entirely satisfactory explanation for the presence of these unusual striations and ring shadows, these 2 cases are reported in detail.

CASE 1. C. W. R., male, white, aged twenty, soldier, born and reared on a farm in central Georgia and, except for a short time in a mill, spent all his time on a farm before enlisting in the Army in October, 1937. He was admitted to the Station Hospital, Fort Benning, Georgia, November 11, 1938, complaining of pain in the chest which he stated was present since his attack of measles a short time after enlisting. His family history is negative. Mother died of "heart trouble," aged forty-nine. Father, fifty-nine years old, is strong and healthy. Two brothers living and well; one brother died of kidney trouble. Two sisters living and well; one died during childbirth. No family history of consanguineous marriage or other pertinent matter.

Previous Personal History. In a letter from the father, information was received that the patient was a strong healthy baby and child, that he had no chronic or lasting illness, and that he did not take any medicine for any length of time. The only significant fact brought out was that when he began to grow he grew very rapidly. He had influenza in 1933 and measles a short time after entering the Army. He injured his right foot when a wagon ran over it when he was eight years old—did not see a doctor, but limped for a long time. No history of venereal disease. Does not drink, but smokes moderately.

FIG. 1. Case 1.

On examination he is seen to be a well nourished young adult; aged twenty, height, 71 inches; weight, 170 pounds. He is lackadaisical but intelligent and cooperative; temperature, pulse and respiration are normal. Posture is good and there is no sign of old rickets. Muscles are soft. The respiratory and circula-

* We regret to announce the death of Colonel Stammel on May 25, 1941.—ED.

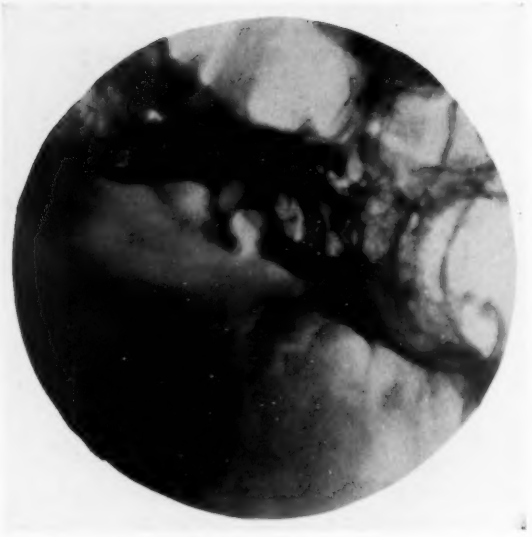

Fig. 2. Case 1.

tory systems are normal. Blood pressure, 100/60; eyes, ears, nose and throat, normal; genitourinary tract, negative. Joints are normal, except for tendency to equinus in right foot. Wassermann and Kahn tests negative on several occasions. White and red cell count normal with no cytological evidence of anemia. Hemoglobin varies between 85 and 95 per cent. Sedimentation rate, 4 mm. in 60 minutes.

Blood Chemistry.

Non-protein nitrogen	27.00 mg. per 100 cc.
Creatinin	1.20 mg. per 100 cc.
Sugar	100.00 mg. per 100 cc.
Calcium	8.2 mg. per 100 cc.
Phosphorus	3.8 mg. per 100 cc.

Blood calcium repeated, Kramer and Tisdal, 8.6 mg. per 100 cc.; blood phosphorus repeated, Bell and Dorsey, 4.2 mg. per 100 cc.; basal metabolic rate, minus 5 per cent.

On making a gastrointestinal examination with barium meal, the multiple concentric striae in the alae of the ilia were noted. This finding was so unusual that a skeletal survey was made, and the following atypical findings recorded. In the skull, the base appeared sclerotic, the posterior clinoid processes thickened and bulbous. The mastoid areas appeared denser than normal, the pneumatic cells very small; the frontal sinuses absent. The bodies of the vertebrae were sharply and densely outlined; within the bodies of which were found the contours of smaller well shaped bodies. All the pelvic bones were affected. The first sacral segment resembled a lumbar vertebra sacralized bilaterally. Paralleling the epiphyses and concentric to centers of ossification were many alternating bands of increased and decreased density. This was particularly striking in the ilia where these concentric striations reminded one, as previously noted, of the growth lines on the back of a clam shell or oyster shell. Above the acetabular cavities these lines coalesced to form bands of sclerotic density. The upper synchondroses of the femurs were thickened and sclerotic, with striations of increased and lessened density extending into the shafts. In the lower third of both femurs just above the condyles there was a definite fusiform swelling of the cortex. Extending upward into the shafts and paralleling the epiphyseal lines were many transverse bands of increased and decreased density. The heads of the fibulas which were thickened showed the same transverse striations. The tarsal naviculars were flattened and sclerotic and had the characteristic appearance of Köhler's disease or osteochondrosis. The third cuneiform bones and the cuboids contained concentric ring shadows. The other tarsal bones

Fig. 3. Case 1.

were normal. The metatarsals and some of the phalanges had cross straitions. The right foot showed marked external angulation of the shafts of the 2nd, 3rd, 4th and 5th metatarsal bones, the result of an old injury. The humeri and the radii showed the same cross striations. In the upper parts of the humeri the shafts were fusiformly thickened. The distal epiphyses of the radii were not fused. The trapezium was the only carpal bone involved. Here a definite double contour was seen. The first metacarpals were striated.

The report of Lt. Col. P. A. Chesser, Dental Corps, is very interesting. It is quoted in full as follows, since a similar condition was not found reported in the literature.

1. A survey of the mouth shows congenital absence of the 3rd molars and lower right central.

2. Incipient caries in the 2nd left and right 1st molars.

3. A deciduous right superior second molar with a small cavity, and an unerupted second cuspid.

4. All anterior teeth show attrition to such a degree that from 3 to 5 cm. of the incisal surface has disappeared, leaving dentine surrounded by a thin matrix of coronal enamel.

Fig. 4 Case 1.

Fig. 5. Case 1. Note striations and sclerosis of navicular bone.

5. The superior bicuspids and cuspids show clinically what might be termed hyperplasia of the enamel. There are circular ridges like the growth lines seen in bark of some trees and shrubs. The ridges show a glistening translucent enamel, while the valleys between are whitish, poorly calcified and indented with small pits. This is observed on the facial surfaces only. Caries is not present in these teeth.

6. Dental films show white spots in all first molars, similar in many respects to the early changes sometimes seen in caries.

7. This condition could be a manifestation of:

(a) Hereditary syphilis.

(b) Dietary and nutritional disturbance seen in pregnancy which causes malformed teeth in the child.

(c) The exanthemata which may delay dental growth.

(d) The effect produced by such diseases as rickets on developing teeth.

8. In general this condition is thought to be a manifestation of some local or general systemic condition which has interrupted the nutrition of the odontoblastic, ameloblastic, cementoblastic tissues.

Case II. A. C. G., male, white, aged nineteen, soldier (private), born in Southern Georgia and

Fig. 6. Case II.

remained on a farm until he enlisted in the Army. He was admitted into the Station Hospital, Fort Benning, Georgia, March 13, 1939, because of an injury to his right foot. His family history is negative. Father died of pneumonia. Mother and five brothers living and well. One brother died of pneumonia, aged nineteen. One killed accidentally, aged twenty-five. Had measles and mumps as a child. Never has had a broken bone. In answer to questionnaire, his mother stated that he was a healthy breast fed baby, did not have any lasting chronic illness and did not take any medicine except for some acute condition. On examination he was found to be a well-developed young man, height 67 inches, weight 139 pounds, with no complaint except some pain in right foot. Physical examination was negative throughout.

Laboratory Examination. Urinalysis, negative. Red cells, 5,180,000; white cells, 10,250. Cytological examination, normal. Blood calcium, 9.8 mg. per 100 cc.; blood phosphorus, 4.4 mg. per 100 cc.; CO_2 combining power, 68. Wassermann and Kahn reactions, negative.

Roentgen Examination. The skull was normal. All the bodies of the vertebrae showed the same double contour described in the first case. The pelvis had the same concentric striation, but not nearly so marked. Whereas in the first case at least eighteen distinct lines could be counted, there were only four and these were widely separated. Both femurs and tibias showed from four to five striations extending well into the shafts. Both first metatarsals were also striated. Typical concentric ring shadows not seen in the tarsals except in the first and second cuneiform bones. The upper epiphyseal synchondroses of both humeri were thickened and sclerotic. Some striations seen in lower metaphyses of the radii and well marked in

Fig. 7. Case II.

Fig. 8. Case II.

lower ends of proximal phalanges. The lower epiphyses of the radii and ulna were not fused. No ring shadows seen in the carpals.

Dental examination, physical and roentgenographic, reported negative. All teeth were present and in very good condition.

In comparing the clinical and roentgen findings in these 2 cases the following points are noted.

Both were strong healthy young adults able to pass the rigid examination for entrance into the Army.

Both were country boys, sons of tenant farmers, from farms in southern Georgia.

Both were reported as healthy breast fed babies and healthy children. Neither had taken any medicine and their early life was uneventful. Case I grew rapidly when he began to grow. Case I has been discharged from the Army. Case II is still in the service and doing full duty with no complaints.

Roentgenographically the following similarities are noted. Concentric ring shadows in the pelvic bones and bodies of vertebrae

Fig. 9. Case II.

Fig. 10. Case II.

and striations in the shafts and epiphyses of the long bones. The findings in the first case were much more marked than those of the second case.

The bulbous condition of the posterior clinoids, the club-shaped enlargement of the upper humeri and lower femurs and tibial heads were absent in the second case.

The distal epiphyses of the radii were not fused in either case. This may be significant.

Neither case had anemia, nor had either shown a tendency to fracture.

In support of the original impression that the first case was an atypical case of Albers-Schönberg's (marble bone) disease, the following excerpts from the literature are noted.

Pirie in his study of the development of marble bone disease says, "The ring shadows in the carpal bones and the iliac bones are early manifestations of marble bones elsewhere." Reynolds, in an edi-

torial, says, "One of the characteristic aspects of the disease (marble bones) is the presence of alternating bands of greater and lesser density arranged parallel to the epiphyseal lines." Karshner's case showed club-like thickening of the posterior clinoids, transverse striations in the long bones, clubbing of the upper humeri and lower femurs. Rodgers, *et al.*, in speaking of the differential diagnosis of lead poisoning in children say, "In many cases of Albers-Schönberg's disease there is widening of the lower ends of the femurs, and the presence of this makes the diagnosis more easy." Case 1 has the ring shadows in the carpal and iliac bones, alternating bands of greater and lesser density parallel to epiphyseal lines, club-like thickening of the posterior clinoids, clubbing of the upper humeri and the lower femurs.

Zwerg and Laubmann in 1936, on the other hand, after a study of all the reported cases of Albers-Schönberg's disease, accepted only 55 as true cases. The following triad of symptoms is necessary before such a diagnosis meets their approval.

1. Generalized endosteal, osteosclerotic changes in the entire skeleton, which are demonstrated at a very early stage.
2. Abnormal tendency to fracture.
3. More or less definite changes in the morphology of the blood.

Cases 1 and 11 do not meet these requirements. Neither case shows any abnormal tendency to fracture and both have normal blood pictures. The other conditions found in the literature which have similar roentgenological bone appearances were all reported in babies and young children and are listed as follows: Endocrine disturbance, hypothyroidism in particular; rickets, scurvy, phosphorus and lead poisoning, and poisoning by other metals such as bismuth, arsenic, strontium and excess medication with vitamin P.

Since rickets is generally considered to be the most common agency producing striations in the shafts paralleling the epiphyseal synchondrosis, it is first considered. Wimberger speaks of relapsing rickets and seeing two or three bands of calcification in the metaphyseal ends of long bones of children, and of the rarity of finding centers of ossification surrounded by a thick band, as in infantile scurvy. Bromer, in the roentgen diagnosis of rickets, says, "Transverse striations, thin fine lines, at varying intervals from the ends of bone are often found. These are not pathognomonic of healed rickets, but are the result of any disease, which at one time has arrested growth." In the 2 cases reported rickets was not seriously considered, since neither case had any stigmata of old healed rickets. Besides, if these striations and ring shadows are the result of old healed rickets, they would be more commonly seen in adult life. The same thought arises regarding other diseases which temporarily cause arrest of growth. Such diseases are common in childhood but concentric ring shadows and multiple striations are not very common in adult life.

Dr. Ralph S. Bromer, who very kindly examined the films, thinks that periodic decreases in the thyroid function is a very likely cause for these cross striations and linear markings in the ilia, and points to the failure of fusion of the distal epiphyses of the radii as additional evidence of hypothyroidism. He referred to Kemkes, who reported 4 children, aged six, five, four and two years, who showed bone pictures identical to those of Cases 1 and 11, which he attributed to hypothyroidism. His conclusions, however, are complicated by the fact that these children all received several series of treatments with phosphorus in cod-liver oil. Regarding the failure of fusion of the distal epiphyses of the radii some authorities give twenty years, others twenty-one years when fusion takes place. However, much confidence cannot be placed in the given age of soldiers, since many give older ages in order to join the Army. Careful examinations into the histories of our cases showed that both boys were reported as being healthy babies and children, and neither one had any lasting illness for which any medication such as cod-liver oil was given. In a personal com-

munication, Schaefer, who with others examined 285 clinically proved endocrinopathic cases, ranging from eight to eleven years of age, 85 of whom showed clinical and laboratory evidence of hypothyroidism, stated that while many of these cases showed striations in the long bones, which they attributed to healed rickets, none showed any concentric ring shadows in the small bones or in the pelvis.

The possibility that these striations, particularly the ring shadows in the carpals and tarsals, are due to scurvy in childhood must be considered. Wimberger (quoted by Bromer) described a characteristic dense edge around the centers of ossification and in the epiphyses of long bones also the same dense edge around the bones of the tarsus. Bromer speaks of four stages in scurvy: In the first stage the appearance of the white line, a broadened dense zone near the diaphyseal line—the zone of temporary calcification. In the second stage, a zone of decreased density just behind the dense broadened zone of temporary calcification. In the third stage the appearance of subperiosteal hemorrhage. In the fourth stage of repair and absorption of hemorrhage, the zones of temporary calcification become broader and denser and double lines of calcification are seen stretching across. This is due to the fact that, as the bone grows the heavily calcified zone of temporary calcification recedes toward the center of the shaft. Wimberger thinks these lines are a measure of growth and are pathognomonic of scurvy. There is a strong likelihood that these lines and shadows in Cases I and II are the result of repeated attacks of a mild form of scurvy in childhood. The clubbing of the lower ends of the femurs and upper ends of the humeri in the first case may be due to old healed subperiosteal hemorrhages of the third stage of scurvy. That mild attacks of scurvy could occur on the farms of share croppers in Georgia and pass unnoticed is not unlikely.

In 1918 Phemister gave a boy four years old a course of phosphorus, and eight months later made roentgenograms of the bones and found a heavy band shadow at the end of the shaft of the femur. The drug was discontinued and four months later another examination was made. Growth had continued and the epiphyses were found beyond the line and a second line was seen in the immediate zone of growth along the epiphyseal line. Examination four months later showed the same line. Phosphorus was again given for five weeks and seven and a half months later another roentgenogram made. At this time three faint lines were seen. One, as he concluded, for each series of treatments. Wegner in 1872 fed phosphorus to growing dogs, cats and chickens and demonstrated dense narrow lines of bone formation about the periphery of the epiphyses and around the centers of ossification. Phosphorus fed to adult animals did not produce this change. That these lines were due to phosphorus administration in our cases is not probable since the parents of both boys stated that they did not receive any medication for any length of time.

To disprove the possibility that these striations are not the result of repeated attacks of chronic lead poisoning would be difficult. In 1924 Minot and Aub demonstrated the storage of lead in the bones, and Park, Vogt and Caffey described the roentgenological appearance of the bones of children and young animals after the ingestion of lead. Caffey's first case, aged eighteen months, showed an increase in density of the periphery of two ossification centers in the carpus, and bands at ends of tibiae and fibulae, which he stated were made up of many narrow bands. Six months later the bands appeared to be fading and replaced by a series of lines at various levels. After thirteen months the lines were deeper in the shafts and the carpal bones were larger with a normal outer periphery, but an inner ring of increased density. Superimposing the film made thirteen months before, during the active stage, showed the inner ring corresponded almost exactly with what was then the peripheral margin of the bone. The distal femora showed the greatest

change while the slower growing bones such as the proximal ulnae, radii and distal humeri showed very little change. Park pointed out that the ingestion of lead affects only those parts that are actually in the process of growth. Rodgers, *et al.*, pointed out the similarity of the effects of lead to those in scurvy, congenital syphilis, Albers-Schönberg's disease, poisoning by vitamin P and elementary phosphorus and the few cases reported of poisoning by strontium and bismuth. Korenchevsky calls attention to the similarity between the effects on the growing bones of phosphorus and arsenic.

Certain features brought out in these reports deserve special comment. Chesser in his dental report in Case I pointed out the ring-like formation seen in superior cuspids and bicuspids. These ridges, as he called them, can be compared with the striations in the long bones. It is significant that the cuspids begin to calcify in the third year and the bicuspids in the fourth and fifth year. In the carpi the trapezium alone showed typical ring shadows. The center of ossification of the trapezium appears at four years. In the tarsi the only typical ring shadows are seen in the third cuneiform bones. This center appears at three years. In the second case the second cuneiforms show the clearest ring shadow. In the first case we may conclude that, whatever condition caused temporary delays in growth, it began after the third or fourth year. That some temporary change in the food or drinking water occurred was thought of; however, roentgen examination of the brother of Case II was negative. The excellent condition of the teeth in Case II precluded the possibility of chronic fluorine poisoning. The pitting of the teeth in Case I was not suggestive of fluorine intoxication either.

Study of the literature reveals that there are almost a dozen conditions which can produce in babies and children roentgen findings similar to Cases I and II. It is rather odd then that they are not seen more often in adults. Possibly more cases are seen but not considered of sufficient consequence to report.

SUMMARY

Alternating bands of increased and decreased density parallel to epiphyseal lines, concentric ring shadows around growth centers, and cross striations in the long bones are not commonly seen in adults.

Two such cases are considered sufficiently rare enough to report in full.

Nothing in the physical examinations, history or laboratory findings furnishes any clue as to the cause.

It is reasonable to suppose that something occurred during the period when the bones were undergoing growth most actively that temporarily caused a delay or cessation of growth.

The most probable condition that may cause this, according to some authorities, is unexplained periods of thyroid hypofunction.

Repeated mild unrecognized attacks of scurvy may also be a plausible explanation.

Also, it is not inconceivable that as babies or children they ingested enough lead or other metal to be deposited in the bones, but not enough to cause severe symptoms.

Lastly, it is not entirely improbable that Case I in particular is an atypical, mild or undeveloped case of marble bone disease.

REFERENCES

1. Aub, J. C., Fairhall, L. T., Minot, A. S., and Reznikoff, P. Lead Poisoning. Medicine Monographs. Vol. XII. Williams & Wilkins Co., Baltimore, 1925. Quoted by Vogt, ref. 15.
2. Bromer, R. S. Roentgen-ray diagnosis of infantile scurvy. Am. J. Roentgenol. & Rad. Therapy, 1928, *19*, 110–125.
3. Bromer, R. S. Rickets. Am. J. Roentgenol. & Rad. Therapy, 1933, *30*, 582–589. Also: Personal communication.
4. Caffey, J. Clinical and experimental lead poisoning: some roentgenologic and anatomic changes in growing bone. *Radiology*, 1931, *17*, 957–983.
5. Caffey, J. Changes in growing skeleton after administration of bismuth. *Am. J. Dis. Child.*, 1937, *53*, 56–78.
6. Editorial. Albers-Schönberg's disease (marble

bones; osteopetrosis). Am. J. Roentgenol. & Rad. Therapy, 1935, *33*, 94–96.

7. Karshner, R. G. Osteopetrosis. Am. J. Roentgenol. & Rad. Therapy, 1926, *16*, 405–419.
8. Kemkes, B. Ueber familiär auftretende Störungen des Knochenwachstums im Röntgenbilde. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1929, *40*, 90–98.
9. Korenchevsky, V. Etiology and Pathology of Rickets from an Experimental Point of View. Medical Research Council, London, 1922, pp. 1–169.
10. Park, E. A., Jackson, D., and Kajdi, L. Shadows produced by lead in x-ray pictures of growing skeleton. *Am. J. Dis. Child.*, 1931, *41*, 485–499.
11. Phemister, D. B. Effect of phosphorus on growing normal and diseased bone. *J. Am. M. Ass.*, 1918, *70*, 1737–1743.
12. Pirie, A. H. Development of marble bones. Am. J. Roentgenol. & Rad. Therapy, 1930, *24*, 147–153.
13. Rodgers, T. S., Peck, J. R. S., and Jupe, M. H. Lead poisoning in children. *Lancet*, 1934, *2*, 129–133.
14. Schaefer, R. L., Strickroot, F. L., and Purcell, F. H. Endocrine implication of juvenile chondro-epiphysitis. *J. Am. M. Ass.*, 1939, *112*, 1917–1919.
15. Vogt, E. A. Roentgen sign of plumbism. Am. J. Roentgenol. & Rad. Therapy, 1930, *24*, 550–553.
16. Wegner. Quoted by Phemister, ref. 11.
17. Wimberger, H. A Study of Developing, Florid and Healing Rickets as Demonstrated by X-Ray Photography. Studies of Rickets in Vienna, 1919–1922. Medical Research Council, Special Report Series, No. 77, London, 1923, pp. 95–114.
18. Zwerg, H. G., and Laubmann, W. Die Albers-Schönbergsche Marmorkrankheit. *Ergebn. d. med. Strahlenforsch.*, 1936, *7*, 95–136.

THE TREATMENT OF MIXED TUMORS OF THE SALIVARY GLANDS BY ROENTGEN RAYS AND RADIUM

By JOSEPH McFARLAND, M.D., Sc.D., F.A.C.P.*
PHILADELPHIA, PENNSYLVANIA

DURING the last twenty-five years I have spent a considerable part of my time in collecting and studying the so-called mixed tumors of the salivary glands and have succeeded in assembling more than 400 cases. Of them more than 100 have recurred—25 per cent. Seventy-one of the tumors had received some kind of treatment by roentgen rays or radium or both, and of them 61 were accompanied by sufficient information to permit them to be included among those used in the following analysis of the results of the treatment.

It seems to be generally accepted among roentgenologists that mixed tumors are extremely radioresistant, but that knowledge seems not to have reached the surgeons who still insist that their cases shall be treated, and some of the cases discussed below are receiving roentgen treatments.

The first essential in endeavoring to appraise the radiation treatment of any tumor is to be sure that the lesion treated is a tumor, and in this case, that it is a mixed tumor. It is therefore of fundamental importance that it be examined microscopically. When this is not practiced, see what may happen:

GROUP A. CASES SUPPOSED TO BE MIXED TUMORS, IN WHICH THE DIAGNOSIS WAS CLINICAL ONLY

I. *Treated with roentgen irradiation:*

a. *The tumor entirely disappeared:*

No. 258. H.O.M., female, white, aged seventy-two. Had a tumor the size of a lemon, of two years' duration on the left side of the face; roentgen treatments were begun on May 13, 1935, and by September 27, 1935, it had entirely disappeared.

b. *The tumor grew smaller:*

No. 256. G.A., female, white, aged twenty-eight. Had a tumor the size of a walnut on the left side of the face. It was repeatedly treated with roentgen rays for five years, when it was "definitely smaller, harder and more movable."

No. 259. J.L., male, white, aged fifty-five. Tumor the size of a walnut on the left side of the face repeatedly treated with roentgen rays for five years, after which it was definitely smaller and more movable.

No. 261. C.C., female, colored, aged thirty-three. Had a tumor six months' duration on the left side of the face, 3 cm. in diameter. It received 1,000 r of roentgen rays, and in a year was "small in size, compared with the size at beginning the treatment."

II. *Treated with radium:*

No. 267. G.E.G., male, white. A parotid tumor on the right side was treated with radium. After a year it is stated in the protocol that "the radium had no effect upon the growth."

No. 326. J.H.S., male, white, aged sixty-seven. Following an attack of typhoid fever ten or twelve years ago, he has had a pea-sized lump behind the lobule of the right ear. He received 2,377 mc-hr. of radium which was thought to have caused "some recession." Unfortunately he died of some other trouble before a second course of treatment was given.

In none of these cases is it certain that the "lump" was the mixed tumor that it was supposed to be. It scarcely seems possible that a mixed tumor the size of a lemon could be made to disappear entirely by roentgen treatments lasting over a period of four months only. It is more probable

* Emeritus Professor of Pathology in the Medical Department of the University of Pennsylvania; Professor of General Pathology in the Temple University Dental School, Philadelphia.

that this was some other kind of swelling. The other 3 cases treated with roentgen rays all suffered some diminution in size, and increase in movability. The 2 cases treated with radium showed no definite improvement.

GROUP B. THESE CASES, CLINICALLY DIAGNOSED AS MIXED TUMORS, WERE PROVED TO BE SUCH BY MICROSCOPIC EXAMINATION

I. *Before treatment by a biopsy examination:*

a. *Treated with roentgen irradiation:*

No. 361. Mrs. H.A., white, aged forty-eight. Had a tumor at the angle of the jaw, on the right side for ten or twelve years. A biopsy showed it to be a mixed tumor. It was treated with roentgen rays for two years, diminished in size but did not disappear, so was excised. It measured 5×3×2 cm.

No. 385. J.T., male, white, aged sixty-five. For four years has had a tumor of the right side of the face that reached the size of a lemon. A biopsy was taken and examined, and the tumor found to be a cylindromatous type of mixed tumor. It was given deep roentgen treatments, and three years later the patient wrote "it does not bother me and does not seem to get any bigger."

b. *Treated with radium:*

No. 303. G.W., male, white, aged thirty-four. Had a walnut-sized tumor on the left side of the face. A biopsy was taken, and the diagnosis of mixed tumor confirmed. No excision was performed, but he was given "heavy treatments" with a radium bomb. The tumor "shrank a little," then resumed its former size and continued to grow. Unfortunately he was lost to the follow-up.

II. *The tumor having been irradiated was excised and examined:*

a. *Treated with roentgen irradiation:*

No. 84. E.M., female, white, aged sixty-five. Thirty-two years before coming to the clinic, she became conscious of a pea-sized "lump" beneath the skin, just behind the left angle of the jaw. It gradually increased until it attained the size of a lemon, when it was "heavily irradiated" with roentgen rays and excised. I examined the patient in 1940 and she has had no recurrence in eighteen years. It was a soft myxoid mixed tumor.

No. 139. M.K., male, white, aged fifty. The tumor was first excised in 1928 and found to be a mixed tumor. In two years it recurred and was given roentgen treatments that seemed to make it a little smaller and more movable. It was then excised a second time. No recurrence in seven years.

No. 215. G.O., male, white, aged twenty. Had a pea-sized tumor on the right side of the face that seemed to be growing. He received three courses of roentgen treatments, but the tumor continued to grow until it reached the size of a walnut, when it was excised. No recurrence in five years.

b. *Treated with radium:*

No. 235. S.P., female, white, aged fifty. For six years she had a tumor on the left side of the face after the extraction of a tooth. It was given ten radium exposures, two or three times a week, after which it became smaller. As she feared cancer she had it excised in 1932 and there has been no recurrence or other trouble since—eight years.

No. 243. S.G., female, white, aged twenty-eight. The patient had a tumor for two years on the left side of the face. It was "given a full course of radium and roentgen rays," then excised. She was discharged, moved and not heard from again.

III. *The irradiated tumor was examined after removal at necropsy:*

No. 253. M.K., female, white, aged seventy-seven. Came into the hospital with a large tumor of the side of the face, supposed to be an ulcerated and infected mixed tumor. She received courses of roentgen treatments in 1934, 1935 and 1936 but the tumor continued to grow and she died of it shortly after the last treatment. At the postmortem no metastases were found. Fragments of the tumor examined showed "mixed tumor."

As it is known that there was a mixed tumor to begin with, these cases afford a better opportunity than those in Group A for judging the merits of the treatment, but all that can be claimed is that in 4 cases the tumor diminished somewhat in size.

GROUP C. IN THESE CASES THE PRIMARY TUMOR WAS EXCISED, MICROSCOPICALLY EXAMINED, AND FOUND TO BE A MIXED TUMOR. LATER WHAT IS SUPPOSED TO BE A RECURRENCE MADE ITS APPEARANCE AND WAS TREATED WITH ROENTGEN RAYS OR RADIUM, WITHOUT ANY CONFIRMATION OF ITS TRUE NATURE

I. *The supposed recurrence entirely disappeared:*

No. 202. C.B.R., female, white, aged thirty-seven. Had for one year a lump the "size of the end of the little finger" at the angle of the left jaw. It was excised and roentgen treatments were given at intervals for five years, when a recurrence was observed. More roentgen treatments were given for fifteen months when no trace of the lesion could be found. In its histology the primary tumor resembled carcinoma.

No. 364. J.P., male, white, aged twenty-nine. Had a small lump in his neck for three years. It was excised and found to have considerable resemblance to squamous cell carcinoma. A month later he had a hard, tender swelling that was supposed to be a recurrence by some, an inflammatory disturbance by others. It was given roentgen treatments—1,200 r—and completely disappeared.

II. *The supposed recurrence grew smaller:*

No. 251. C.D., female, white, aged sixty-one. In 1926 observed a tumor that was promptly excised. Diagnosis "mixed tumor." In 1931 there was a recurrence that was treated for four months with roentgen rays and "some shrinkage effected." She died that year, cause not known. No necropsy was performed.

No. 384. I.L., female, white, aged twenty-eight. Tumor of three years' duration beneath the angle of the right jaw. It was firm and of walnut size. It was excised and found to be a soft, myxoid variety of mixed tumor. Three years later the incision scar "became heavy" and three roentgen treatments were given. The scar was then not so noticeable as before.

III. *The supposed recurrence apparently stopped growing:*

No. 155. Mrs. G., white. Had a tumor removed. It proved to be a soft, myxoid mixed tumor, and recurred in a month. A letter from the patient's family doctor says that "under x-ray treatment it has been controlled for thirteen years."

No. 380. T.B., male. Had a supposed mixed tumor removed in a distant city. Ten years later there was a recurrence, and in a Philadelphia hospital an effort was made to excise it. The surgeon found it impossible to get it all out, and a fragment the size of a lima bean remained. He was given nine roentgen treatments, and in four years the fragment has not increased in size.

IV. *It is too soon to note any effect of the treatment:*

No. 162. Mrs. C.E., aged fifty-six. Tumor of one year's duration the size of a bantam's egg on the right side of the face. It was excised, recurred in seven years, and is now being treated with roentgen rays.

No. 368. M.F., female, colored, aged fifty-five. The tumor on the right side of the face was of six years' duration before it was excised and found to be a myxoid mixed tumor. It gradually grew again, and the recurrence is now being treated by deep roentgen therapy.

No. 370. R.S., female, white, aged forty-three. She had for many years a tumor of the left side of the face that grew to the size of a walnut. It was excised, found to be a chondroid mixed tumor, and is now being treated with roentgen rays.

The cases in this group closely parallel those in Group A. It is *supposed* that the tumor treated is a mixed tumor, and the probability is greatly increased by the fact that its presence had been preceded by a

mixed tumor, but there was no certainty that it might not be some other and altogether different kind of swelling. Note the complete correspondence between Cases No. 258 and 264 in Group A and No. 202 in Group B. In each the swelling under treatment completely disappeared, which none of the others ever did. It would seem as though these 3 cases were of some other kind of morbid condition that may have been cured by the treatment or might have recovered without it. In the other cases there was only reduction in size and increased movability, or a cessation of growth.

It seems worth while to call attention to some peculiarities of the mixed tumors that may explain these seeming benefits, without attributing them to the treatments given. In the first place, many of the patients whose tumors were never treated with roentgen rays or radium assert positively that the size of the tumor varies, sometimes being a little larger, and sometimes a little smaller and that the tumors sometimes seem to grow rapidly, then stop and then sometimes shrink to a smaller size. This may depend upon conditions arising in the tumor or outside of it. Thus pressure upon the salivary ducts may cause obstruction with retraction of saliva in the glandular ducts by which portions of the gland adjacent to the tumor and mistaken for part of it may be brought into prominence, to return to the normal when the pressure is relieved and obstruction overcome. Again cystic changes in the tumor, followed by absorption of some of the fluid, may cause variation in size. The tumor sometimes becomes harder, probably because of hyperemic or inflammatory conditions about its bed. When such are relieved there seems to be a reduction in size and an increased movability.

In the second place the growth of mixed tumors is very variable. In general it takes about five years for one to reach the size of a walnut and about ten years to reach the size of a lemon, but there are many cases in which for a few years the tumor grows, and then stops growing for years, later to begin again.

With these conditions in mind the certainty of the small benefits attributed by the patient and the operator to the treatments administered become somewhat doubtful, at least.

GROUP D. CASES IN WHICH THE TUMOR HAVING BEEN EXCISED, MICROSCOPICALLY EXAMINED AND FOUND TO BE A MIXED TUMOR, ROENTGEN RAYS OR RADIUM WERE EMPLOYED FOR THE PURPOSE OF PREVENTING RECURRENCE

I. *The operation wounds having healed, patients were discharged from the various hospitals and never heard from again. All attempts to "follow-up" failed, and nothing more is known about them:*

a. *Treated with roentgen irradiation:*

No. 123. K.A., female, white, aged fifteen. Tumor of two years' duration and the size of an egg. It was excised, then treated with roentgen rays.

No. 130. H.N., male, white, aged thirty-one. Left side submaxillary tumor of five years' duration. It was excised, then treated with roentgen rays.

No. 177. H.P., female, white, aged thirty-five. A tumor of the right side, of pecan size, and only six weeks' known duration. It was excised, then treated with roentgen rays.

No. 232. M.M., female, white, aged forty-seven. This is the only sublingual tumor in our collection. It was of almond size, of three years' duration, and on the right side. It was excised, then treated with roentgen rays after which the patient was lost to "follow-up."

No. 244. H.F., female, white, aged thirty. The patient had a tumor for three or four years on the right side of the face. After it had been excised in the dispensary, she was given roentgen treatments, and thereafter was lost.

No. 298. J.K., male, aged forty-three. For two years had a tumor in the left side of the neck that became as large as a walnut. It was excised, given roentgen treatments, and the patient was lost.

b. *Treated with radium:*

No. 377. E.G., female, white, aged forty-nine. Had a painless swelling beneath the angle of the jaw for two years, when it seemed to grow larger, was excised, examined and found to be a cellular variety of mixed tumor. It was then treated with 50 mg. of radium, after which the patient went away and was never heard from again.

II. *The patients were followed for varying lengths of time, until they died or were lost, no recurrence having been detected in any case. This might be looked upon as the most important group from which to estimate the value of irradiation in preventing recurrence, yet, in reality, nothing can be learned from it because (1) only 25 per cent of the tumors operated upon do recur under any circumstances; (2) the average interval between operation and recurrence, as nearly as it has been possible to calculate it is seven years, only half of these cases having been followed that long, and (3) recurrence may take place twenty, thirty or even fifty years (our longest interval is forty-seven years) after operation, without the aid of roentgen rays or radium.*

a. *Treated with roentgen irradiation:*

No. 20. H.D., female, white, aged forty-four. Fifteen years after an attack of typhoid fever, she noticed a small tumor below the angle of the right jaw. It grew slowly until she fractured her shoulder, a short time ago, since when it has grown to the size of a cantaloupe (patient) or orange (surgeon). It was excised. Three years later—why the treatment was so long deferred is uncertain, except that she feared cancer of which a sister had died—she was given a long course of roentgen treatments. She died *ten years* later, not having had any recurrence of the tumor, which was a myxoid mixed tumor.

No. 133. A.O.L., female, white, aged thirty-one. Tumor of five years' duration on the right side of the face. Two operations were performed for its removal, and it proved to be the soft myxoid type of mixed tumor. After the second operation she was given roentgen treatments. There has been no recurrence in *seven years*.

No. 178. Mrs. F.S., white, aged thirty. A walnut sized tumor of two years' duration was excised from the right side of the face and proved to be the soft myxoid type of mixed tumor. It recurred in about a year, when a second excision was performed, and a course of roentgen treatments carried out. There has been no further recurrence in *seven years*.

No. 180. L.D., female, white, aged sixty. Submaxillary tumor, 6 cm. in diameter, of one year's duration, on the left side. Excised and examined it was very cellular, and some thought it a carcinoma of the submaxillary gland. It recurred in two years, and roentgen treatments were begun. *Four months later* when the tumor was a little smaller (?) she died of an intercurrent affection.

No. 214. Mrs. I.E., white, aged fifty-five. Had a tumor of the right side of the face for fifteen years. Two years ago she was given a course of roentgen treatments with no appreciable benefit. The tumor was then excised, and there has been no recurrence in *six years*.

No. 217. Mrs. E.B., white, aged fifty-one. A walnut-sized mixed tumor was excised from the right side near the angle of the jaw. She was subsequently given roentgen treatments, and there has been no recurrence in *four years*.

No. 240. E.R., female, aged twenty-six. A tumor of six years' duration was excised, microscopically examined in 1935, and was found to be a myxohyaline and edematous mixed tumor. Then roentgen rays were applied and there had been no recurrence to 1939—*four years*.

No. 242. M.M., male, aged fifteen. For six months had a lump the size of a hazelnut in the right side of the neck. It was excised and recurred within six months, so that a second nodule was excised. The sections were described as "sarcoma of the parotid" by two pathologists. He was given courses of roentgen treatments between the first and second operations. Since the second operation there has been no recurrence in *eight years*. The patient, however, has had a goiter operation since.

No. 269. Mrs. L.T., white, aged fifty. A tumor 1.5 cm. in diameter was excised from the left side of the face where it had been slowly growing for about a year. It was peculiar—adenomatous and angiomatous—but regarded as a variation of mixed tumor. She was given six roentgen treatments, and there has been no recurrence in *five years*.

No. 286. E.R.M., female, white, aged forty-one. Had a submaxillary lump for three years. It was excised, shown to be a typical myxoid mixed tumor; roentgen rays were applied. No recurrence in a year.

No. 305. A.M., female, white, aged seventy-three. Had a submaxillary tumor for two years. It was excised in May, 1931, and shown to be a cellular mixed tumor with squamous epithelium and some pearls, very little glandular, mucous or other tissue. She was given five roentgen treatments. There had been no recurrence in 1939—*eight years*.

No. 314. R.H., male, white, aged twenty-eight. A marble-sized mixed tumor was excised from the left side of the face, where its presence has been observed for one year. He was given five courses of roentgen treatments and there has been no recurrence in *five years*.

No. 350. M.B., female, white, aged fifty. Had a soft myxoid mixed tumor excised in April, 1936. She was "x-rayed" for some time. *Three years* later there was no evidence of recurrence.

No. 355. A.D., male, white, aged forty-seven. Had a tumor of the right parotid for "several years." It was excised, found to be a highly myxoid mixed tumor, and the patient was given ten postoperative roentgen treatments. In *one year* there had been no recurrence.

No. 367. B.B., male, white, aged eighteen. Two and a half years after discovering an enlargement in the left parotid region, he had it excised but it could not all be removed, and the growth continued for four months longer when it was again operated upon, and again only removed in part. He was then given four or five roentgen treatments after which there was no further growth or recurrence and he improved—*one year*. Microscopic examination of the tissue removed showed a mixed tumor.

No. 369. M.O., male, white, aged fifty-five. For two years has had a small hard lump in the right "submaxillary fossa" that gradually increased to the size of an egg. It was excised, roentgen treatments were given and there has been no recurrence in *one year*. Histologically this was a soft myxoid mixed tumor.

b. *Treated with radium:*

No. 16. F.S., male, white, aged twenty-two. At his first appearance at the hospital he showed a tumor of the right parotid region said to be of only six months' duration. It was excised and proved to be a chondroid variety of mixed tumor. In three years it returned, and in eight years had grown so that the patient desired a second operation. The tumor was given radium treatments for some six months, then excised. There had been no recurrence in *three years* when the patient was lost to the follow-up.

No. 46. Mrs. A. M., white, aged thirty-six. In 1914 a somewhat atypical mixed tumor was operatively removed from below the left ear. It measured 2.5×2.1 cm., and the microscopic diagnosis was "cylindroma." In answer to letters sent from time to time she has given the following information: "The lump returned in nine years and three months. I haven't had another operation, but had radium treatments at different times for six months." In December, 1924, she said: "There is a little lump yet at the right end of the jaw." In March, 1931, she wrote, "It is just the same size as it was in 1923—sometimes I think it is a little larger." In 1939: "I think the lump is a little larger, about the size of a small marble now."

III. *The tumors after excision, microscopic identification and radium or roentgen treatments did recur:*

a. *After treatment with roentgen irradiation:*

No. 61. A.C., male, white, aged twenty-five. In 1916 discovered that there was an almond-sized tumor on the right side of the face. It was thought to be a lipoma and was removed. Something began to

grow in the same place, and in 1922, when it was as large as a walnut, it was again excised and found to be a chondroid type of mixed tumor. He next had a course of roentgen treatments, and there was no recurrence until 1936—*fourteen years*—when he found that there was a small pea-sized nodule in front of the tragus of the right ear, a lima bean-sized nodule above and anterior to it, and a third little nodule at the angle of the jaw. For these he received two roentgen treatments. There has been no change in his condition for two years.

No. 236. Mrs. C. C., white, aged fifty-three. First came to the hospital in 1930 with a tumor the size of a marble. It was treated in 1935 by excision followed by roentgen treatments. The excised tissue showed the tumor to be the acinous variety of mixed tumor. In 1936 a recurrence was excised, in 1938 a second and in 1939 a third recurrence was excised.

No. 345. T.G., male, white, aged twenty-six. For two years the patient had a tumor below the ear, on the right side, 2×1 cm. in size. It was excised in 1934, but in two months had recurred and attained its original size. It was now treated with roentgen rays and "reduced in size." A second course of roentgen treatments reduced it to "a cartilaginous mass." A year later, 1935, there was a new recurrence that was excised, but immediately recurred. In 1936 the right carotid artery was ligated and a block dissection of the neck performed. The pathologist reported "atypical parotid tumor," and I have examined the tissue and believe that to be correct. Amid great quantities of dense cicatricial tissue, islands of mixed tumor tissue were encountered. In 1937 there was recurrence in the scar and a node was found in the neck. When it was excised and examined, it proved to be a chronically diseased lymph node, without tumor. The patient died in Panama in 1939, but of what could not be determined.

Almost any one will probably agree that nothing can be learned from the cases in Group D I, but with respect to Group D II there may be differences in opinion due to wishful thinking on the one hand and insufficient acquaintance with mixed tumors on the other.

To the wishful thinker with the usual limited experience with mixed tumors, it seems as though there could be no doubt of the efficacy of roentgen rays or radium in preventing or postponing the recurrence of an excised tumor, when he sees the years pass and no tumor reappear—2 cases for four years, 2 cases for five years, 1 for six years, 2 for seven years, 2 for eight years, 1 for ten years and 1 for eighteen years. If this does not prove the case, what kind of proof can one have?

But to one familiar with the vagaries of these tumors and in possession of data regarding a large number of cases, it proves nothing, for the tumors do quite as well, and often much better without any treatments by roentgen rays or radium. Table 1 shows this very emphatically. In the first column are given the case numbers of the patients treated, showing the years without recurrence, and in the second column an equal number of cases that never received either roentgen rays or radium but have enjoyed much longer periods of exemption from recurrence. But the present exemptions enjoyed by the treated cases in column 1 must not be regarded as permanent for in column 3 are shown the years that elapsed after excision in 11 cases that did eventually recur years after all danger of further trouble was supposed to have been long past.

When the whole series of 100+ recurrent cases is considered, we find a number that are said to have recurred "immediately," some in which recurrence was postponed for thirty years or more, and an average delay of about seven years. In column 1, from which some deduction as to benefit seems possible, it is found to be impossible because two-thirds of the cases have not yet completed the average interval before recurrence is to be expected, and only 4 cases have exceeded it.

Table I

Cases Treated with Roentgen Rays or Radium		Years of Exemption from the Tumor	Cases Treated by Excision only No Roentgen Rays or Radium	
Without recurrence	With recurrence		Without recurrence	With recurrence
Case 180: 355: 367: 369	236: 345	1		
Case	49	2		
Case 16: 350		3		
Case 217: 240		4		
Case 269: 314		5		
Case 214:		6		
Case 178: 133		7		
Case 242: 305		8		
		9	Case 73	Case 46: 51
Case 20		10	Case 70	
		11	Case 30: 36: 75	
		12		Case 90: 127
		13	Case 23: 25: 34: 69	Case 319
	61	14		
		15	Case 19: 68: 74	Case 88
		16	Case 67: 72	Case 45
		17		
Case 84		18		Case 191
		19		
		20	Case 12	
		21		
		22	Case 1	
		23		
		24		
		25	Case 6	
		26		
		27		
		28		
		29		
		30		Case 50
		31		
		32		Case 250
		33		
		34		
		35		
		36		
		37		
		38		
		39		
		40		
		41		
		42		
		43		
		44		
		45		
		46		
		47		Case 318
		48		
		49		
		50		

Furthermore, in spite of the treatment, the tumors often do recur as is shown by Group D III, where the details of 4 such cases are given. Twenty cases that did not (yet) recur and 4 cases that did recur after treatment, gives the percentage of recurrence as 16.6, as compared to the whole series of 400 cases with 100+ recurrences, which equals 25 per cent. This difference might be interpreted to mean that the cases treated with roentgen rays and radium enjoyed a gain of 9 per cent, but only by those inattentive to the general facts concerning recurrence dwelt upon in the preceding paragraph.

There is, therefore, no evidence to show that postoperative roentgen or radium treatment of mixed tumor cases exerts any influence in preventing or postponing recurrence.

TREATMENT OF MALIGNANT SALIVARY GLAND TUMORS WITH ROENTGEN RAYS OR RADIUM

A special contribution to the nature of these tumors is contemplated, so that no more will be said at present about that phase of the problem than seems absolutely necessary. It is important to realize, at the outset, that the so-called malignant tumors are not all of the same kind. It is possible that they may include any of the following:

1. Tumors arising from the salivary glands themselves:
   a. Mixed tumors of rare varieties, cellular structure, and persistent recurrence, purely local, not metastatic. These may be cured by one or more excisions, or they may destroy more and more tissue by infiltration until hemorrhage, infection or extension to the brain kills the patient.
   b. Mixed tumors that may have become carcinomatous with all their clinical manifestations including metastasis.
   c. Primary carcinoma of the salivary glands.
2. Tumors arising from structures adjacent to the salivary glands:
   a. Branchiogenic carcinoma.
   b. Secondary carcinoma of cervical lymph nodes.
   c. Primary carcinoma of the skin over the parotid gland.

   The tumors of this class may be easily identified and no confusion arise so long as they are small, but as they grow and infiltrate they may amalgamate themselves with the salivary gland, so that it is impossible any longer to determine the primary or original seat of the disease.

The tumors in Group E, that follow, were all declared to be "cancer" or "adenocarcinoma," or "carcinoma" by one or more pathologists, and received their roentgen or radium treatments upon that basis. The different categories into which they have been divided will show that not all belonged to the carcinomatous tumors as such are ordinarily understood.

GROUP E. CASES IN WHICH THE HISTOPATHOLOGIC APPEARANCE OF THE TUMOR WAS SUCH AS TO SUGGEST CARCINOMA. THESE TUMORS WERE ALL CALLED "MALIGNANT" BY ONE OR MORE PATHOLOGISTS, AND SOME WERE UNRESERVEDLY DECLARED TO BE CARCINOMAS

I. *The histopathological appearance and clinical behavior of the tumors did not correspond as these tumors did not behave as carcinomas ordinarily do:*

1. *Because of their extremely long preoperative duration:*

No. 88. M.H., female, white, aged sixty-five. In 1909 something that she described as a "chest tumor" or "cheese tumor" was excised from the right side of her neck. Thirteen years later in 1922, a new lump appeared in the same place and in two years grew to the size of an orange. She was carefully treated with radium, but a roentgenogram of the chest made in 1925 showed what was thought to be metastasis to the lungs, and there were two nodules in the neck.

She then failed to appear for more treatments, probably because she was working. Inquiry made in 1926 discovered that she had had a recurrence, and was now dead. No necropsy was done. The microscopic section of the large tumor of 1922 resembled carcinoma, and no connection between it and a salivary gland could be discovered. There was no proof that the nodules in the neck and lungs were metastatic tumors.

No. 249. E.A.T., male, white, aged sixty-six. About 1910 discovered a lump under the angle of the jaw on the left side. It grew very slowly for ten years or so, attaining the size of the end of the thumb, then proceeded to grow more and more rapidly and to extend into the back of the mouth. A biopsy showed mixed tumor with much carcinomatous-like structure. It was treated with the radium pack. He became very ill after the treatment, had pain and difficulty in swallowing and died in twenty-two days.

No. 252. W.K., male, white, aged sixty-eight. This patient had a tumor on the right side of the face for fifteen years before it was excised in 1934, together with some adjacent lymph nodes. The diagnosis was "carcinoma of the parotid with metastasis to the lymph nodes." Another pathologist studied the material carefully and reported, "undifferentiated carcinoma," declaring that there was nothing to show that the disease began in the parotid or that it was "malignant change in a mixed tumor." In two years the patient returned, and three lymph nodes were dissected from his neck. He was given roentgen treatments but died in November, 1936. Some would assume that this was a mixed tumor that had "become carcinomatous."

2. *Because of the extreme youth of the patient at the time of first appearance:*

No. 115. S.G., female, white. When ten years old a tumor well encapsulated and attached to the parotid gland was excised. The pathological report upon this tissue was adenocarcinoma, and she was given irradiation with low voltage roentgen rays. There was a recurrence in four months and a second excision was performed. The pathological report was again adenocarcinoma, and she received radon followed by radium packs to the neck. Six months later there was another recurrence which was excised, together with several lymph nodes. The pathological report was "spinous cell carcinoma without cornifications, and metastasis to a lymph node." More radon seeds were implanted and radium packs again applied. A third recurrence was operated upon two years later. A year later what looked like a small cyst was snipped off by the surgeon with curved scissors, a month later a second was similarly removed and the base fulgurated; then four months later another cyst was treated in the same way and followed by high frequency roentgen rays. *Five years* have now passed with no further recurrence, and she has developed into a healthy appearing young woman.

No. 127. M.D., female, white, aged forty-one. The mother of the patient first observed the tumor on the right side of the face when she was only four years old. The first operative removal was performed when she was fourteen. There was an interval of twelve to fourteen years before recurrence was detected and promptly excised. Four years later a second recurrence was excised. Six years passed, and then another recurrence was treated with roentgen irradiation for a year and a half, but the tumor continued to grow and the next year, when the size of a walnut, it was exposed both to radium and to roentgen rays. As it did not seem to lessen in size, excision was performed and the bed of the tumor seared with a high frequency knife. In ten months there was a recurrence the size of a hen's egg that was also excised. She died the next year. The histopathology of this tumor bore no resemblance to a mixed tumor—the early lesions were not examined and it was believed by several pathologists to be a carcinoma.

No. 197. E.S., female, white, aged forty-five. Had a tumor on the left side of the

face since childhood. It was first treated by "ligation" when she was ten years old. Various attempts at removal have been made without success as it persistently recurred. The tissue removed at an operation in 1929 was exactly like carcinoma in microscopic appearance. She was given roentgen treatments, but in 1934 "a tumor the size of a small pea appeared below the original one . . . the doctor removed the same under local anesthesia, since when there has been no further trouble"—*five years*.

3. *Because the tumor remained local and gave no metastasis to the lymph nodes or lungs:*

No. 85. M.S., female, white, aged forty-five. In 1905, in Russia, this woman had some kind of a tumor excised from a position in front of the right ear. Nothing happened for ten years, then in 1915, in Philadelphia, a recurrence was excised. No microscopic examinations are known to have been made of these tumors. In January, 1923, a second recurrence was excised at a third hospital, and recurrence was immediate. In October, 1923, in a fourth hospital, a small, soft, fleshy tumor mass just anterior to the right ear was excised and roentgen treatments instituted. This tissue was examined, and the first diagnosis was "parotid tumor, papilliferous, like carcinoma"; afterwards it was corrected to read "carcinoma." In spite of the roentgen treatments there was recurrence and in 1924 it measured 1×7/10 inches. Tissue studied in another (fifth) hospital was diagnosed "adenocarcinoma." She entered a sixth hospital in 1926, where a biopsy was taken but the tissue proved to be only parotid gland. "The growth rapidly enlarged, spreading on the head and behind the ear," and she died May 1, 1926, no necropsy being permitted. No metastases were at any time observed.

No. 127. M.D. This case was described above (see E 2).

No. 220. Mrs. L.D., white, aged sixty-two. The tumor had been recognized only one month, and was only the size of a walnut when it was first treated by excision in 1925. It was a small encapsulated nodule of reddish color measuring 2.5 ×2×1.75 cm. Histopathologically it was described as an adenocarcinoma. It recurred and in 1927 the patient sought advice at a second hospital where it was again excised, and the operation followed by radium treatments. The patient died at home, the same year, no necropsy having been made.

4. *The tumor was metastatic:*

No. 206. Mrs. M.S., white, aged thirty-seven. In 1930 a tumor the size of a pecan, supposed to have "followed impetigo and keloid" was excised from the left side of the neck. In 1935 there was recurrence and roentgen rays were applied. It "became smaller and healed." In 1928 there was a "new rapid growth" and another excision after which radium treatments were applied. The tumor continued to spread and the patient died in 1930. Necropsy showed the death to be due to "papillary carcinoma with metastasis in the neck." Microscopic examination of the tissues justified the diagnosis.

Of these 9 malignant tumors, 6 began in adult life and in spite of energetic treatment by excision, roentgen rays, radium, radon seeds and radium pack, *all died*. Of the 3 juvenile cases, 1 died, and 2 have lived for five years since the last treatments were given. What the final outcome is to be remains to be seen.

That five years' exemption from recurrence is by no means unusual is shown by the following cases that were treated by the knife only, and never received either radium or roentgen treatments:

No. 76. J.D., male, white. A tumor that several pathologists were agreed was a carcinoma of the parotid, was excised from the side of the face where it had been observed for two years. Within a year it recurred and had become as large as the primary growth. It was again excised, since which operation there has been no recurrence or other trouble for *eighteen years*.

No. 191. G.F., male, white. After the excision of what is described as a "parotid

cyst," fifteen years passed before a tumor appeared. It was excised, microscopically examined, pronounced "carcinoma," but since that second operation there has been no recurrence or further trouble for *twelve years*.

The cases considered in this analysis have been treated in fifteen different hospitals in and about Philadelphia, and must constitute at least three-fourths of all cases of mixed tumors treated in this city. Some of the cases were at different times in several different hospitals, so that the treatments must have been administered by fifteen or twenty different radiologists, by a variety of techniques, and over a sufficiently long time to have permitted all varieties of treatment to be tried. But in spite of all the opportunities for benefit thus afforded, the results of treatment by roentgen rays and radium have uniformly failed. The so-called benign cases seem to have behaved like untreated cases of the same kind, so far as any deduction was possible, and no difference whatever obtained in the end-results of the malignant cases.

It seems justifiable to conclude, therefore, that it is not worth while to put the patients to the expense and discomfort of treatments that are of no value.

DERMATOSES ASSOCIATED WITH ROENTGEN THERAPY

By S. G. CASTIGLIANO, M.D.
American Oncologic Hospital
PHILADELPHIA, PENNSYLVANIA

THE usual reactions of the skin following radiation therapy are generally well understood by both radiologists and dermatologists. Described in the literature, however, are various dermatoses appearing outside the portals of irradiation, associated with roentgen therapy, some of which are apparently little understood. In the vast literature that has developed in the past twenty years on the subject of roentgenology, I could find no collective review of the various cases reported in the literature.

Perhaps the most common type of dermatitis spreading or appearing beyond the confines of the roentgen treated area is a skin change which resembles acute infectious eczematoid dermatitis. I have seen this condition occasionally and because of the early confusion which frequently arises in diagnosis, I should like to present and discuss briefly 4 cases, and to review other generalized skin reactions following roentgen therapy which have been reported periodically in the literature.

FIG. 1. Case I. Showing the dermatitis on the lateral aspect of the thigh extending up into the groin. The dermatitis continued to spread to involve nearly the entire lateral aspect of the thigh. The scarred draining lesion can be seen to the right.

The following 4 cases illustrate different aspects of the condition in question observed while treating neoplastic diseases in this clinic. This dermatitis may occur unrelated to roentgen therapy, appearing postoperatively in patients with draining ulcers or sinuses (Case I). The dermatitis may appear associated with an exudative roentgen dermatitis, with or without a draining lesion (Cases II and III). It may also appear associated with an ulcerative roentgen dermatitis (Case IV). It may vary from abortive forms (Case III) subsiding in a few days to those having a protracted course lasting weeks.

REPORT OF CASES

Infectious Eczematoid Dermatitis Unassociated with Recent Roentgen Therapy.

Case I. A white man, aged forty-nine, presented himself in July, 1938, with a fungating neoplasm of ten months' duration on left thigh. Examination revealed a sessile neoplasm, irregularly kidney-shaped, which measured 10×7 cm. and was elevated about 2 cm. Laboratory studies and roentgenograms were not noteworthy. The blood Wassermann reaction was negative. The lesion was excised. A microscopic report of melanoma was made. The indolent ulcer healed slowly and was therefore stimulated with pinch grafts. On November 26, 1938, an eczematoid rash developed about the draining ulcer (Fig. 1). Inasmuch as the patient had made plans to return home for the Christmas holidays, he was referred to his family physician for treatment. This weeping, branny dermatitis spread to involve practically the entire outer aspect of the thigh. The widespread reaction had regressed by January 17, 1940, although a small area persisted.

Infectious Eczematoid Dermatitis Associated with Roentgen Therapy and a Draining Lesion.

Case II. A white woman, aged sixty, mother of four children, presented herself for examination because of a lump of eighteen month's

duration in her right breast. Her history is essentially irrelevant. She never had attacks of exudative skin rashes, urticaria or any allergic diseases. She had typhoid fever and scarlet fever during adolescence. A diagnosis of carcinoma of the breast was made. The patient did not have the skin suggesting an exudative diathesis. The examination otherwise revealed no noteworthy findings. The laboratory studies, including the blood Wassermann, were all negative.

Following a course of deep roentgen therapy, a simple mastectomy was done. A microscopic study confirmed the diagnosis of carcinoma.

Several days postoperatively, the central portion of the wound broke down and a discharging sinus about 2 cm. in diameter resulted. Thirteen days after the operation, roentgen therapy was instituted, but discontinued nineteen days later. No portal received over 1,500 r of deep roentgen therapy. Forty-two days postoperatively the sinus had closed and a shallow ulcer formed. The skin about the incision was reddened. Immediately surrounding the ulcer the skin was edematous, denuded and weeping. Following treatment with benign ointments, improvement took place. Five weeks after irradiation,

Fig. 2. Case II. Showing an eczematoid dermatitis involving the thorax, neck, and arms of a woman, after mastectomy. Drainage had been profuse. Roentgen therapy had been given five weeks before.

the patient presented a marked dermatitis involving the skin of the right anterior and lateral chest wall, extending far beyond the limits of the treated area (Fig. 2). The advancing edge of the dermatitis was elevated and sharply demarcated from the normal skin. The patient complained of a distressing pruritus and a burning sensation. The blood showed no changes from previous examinations. No polymorphonuclear eosinophilic leukocytes were counted in 200 cells. The temperature ranged from 98.6 to 100° F., returning to normal in nine days. Smears were made from the lesions and gram-positive cocci were found in clusters and short chains. A patch test on healthy skin using

Fig. 3. Case III. Showing the dermatitis spreading beyond the portals of treatment. The portals are marked.

the discharge from the ulcer produced a raised pruritic, erythematous area in twenty-four hours. This mild reaction subsided in several days. A patch test, which was done after irritating the normal skin with an applicator, produced a more pronounced reaction, but again subsided in about ten days.

Abortive Form of Infectious Eczematoid Dermatitis Associated with Roentgen Irradiation.

Case III. A woman, aged sixty-three, presented herself in July, 1939, with a lesion of four years' duration inside the cheek. She had received various forms of treatment elsewhere, which were ineffectual. A diagnosis of carcinoma was made. The blood Wassermann reaction was negative. The blood showed only a mild secondary anemia. Roentgenograms of mandible and other studies were normal. Microscopic diagnosis of biopsied material was squamous cell carcinoma Grade 1. Treatment consisted of 4,200 r, deep roentgen therapy, generated at 200 kv. (peak) and 25 ma. The target-skin distance was 50 cm. and the filtration 0.5 mm.

copper and 1 mm. aluminum. The patient received 300 r daily, alternating between two portals. One field measured 6×9 cm. and the other 4×9 cm. The treatment ended August 16,

Fig. 4. Case III. Front view.

1939. On completion of treatment, the roentgen erythema was of average intensity. A fairly marked irradiation reaction with crusting and weeping of the skin had developed by October 1, 1939. Treatment consisted only of topical applications of yellow petrolatum. By November 10, 1939, the skin reaction had largely subsided although some slight weeping persisted. On December 1, 1939, the patient presented an infectious eczematoid dermatitis spreading beyond the confines of treatment at all points. Questioning disclosed that itching, burning and redness of the skin were first noticed about the portals of treatment ten days before, and slowly spread. The redness became more intense and the skin began to weep. This dermatitis had a vivid red background. The advancing edge, although definite, was not raised nor sharply demarcated (Figs. 3 and 4). The patient complained of severe burning and itching. The blood was normal except for the secondary anemia, which was more marked. No eosinophilia was noted. Treatment consisted only of nupercaine ointment. The intense reaction subsided in one week, although a residual widespread dermatitis persisted for another two weeks.

Several attempts to repeat roentgen therapy had to be discontinued because of a prompt recurrence of the dermatitis immediately following two or three treatments given at the rate of 100 to 200 r daily.

Infectious Eczematoid Dermatitis Associated with Ulcerative Roentgen Dermatitis.

Case IV. A married, nulliparous white woman, aged sixty-one, presented herself for examination. Two years before a left radical mastectomy had been performed elsewhere. On examination, a large, firm mass was palpable in the left supraclavicular region. The left hand, forearm and arm were swollen. The axilla presented several large, fixed glands. No definite evidence of distant metastases could be found. The blood picture was normal.

Three courses of deep roentgen therapy were delivered to the areas of recurrence. The supraclavicular region received a total of 9,900 r to four portals over a period of nine months. Brisk reactions followed each course of treatment, but subsided, leaving the skin in good condition. Complete clinical disappearance of the massive recurrences followed, but the swelling of the upper extremity remained unchanged.

The patient returned twelve weeks after the last treatment, complaining of increased swell-

Fig. 5. Case IV. The delineated, triangular area, *B*, represents approximately the last portal of therapy. The irregular area, *A*, is the beginning ulcerative irradiation dermatitis. Note the eczematoid dermatitis spreading irregularly far beyond the limits of treatment six days after onset.

ing of the arm. Because of the patient's distress, an additional course of deep roentgen therapy was instituted. This treatment was delivered to two portals, most of which overlapped the previously treated supraclavicular area. A pro-

tracted, intense reaction followed which slowly subsided, but did not completely clear. Thirteen weeks after termination of treatment, the development of an irradiation burn (ulcerative dermatitis) was apparent. The ulceration increased in depth and grew peripherally. The skin immediately surrounding the ulcer became edematous, angry red. Palpation everywhere over this region was exquisitely tender. Discharge from the ulceration was profuse. The edematous and reddened area immediately about the ulcer began to spread and in six days a typical eczematoid dermatitis had extended far beyond the area of treatment (Fig. 5). The patient was admitted to the hospital.

Within a period of four days after admission, an itching, burning, eczematoid dermatitis had spread to involve the neck, shoulder, upper back, anterior thorax, including most of the large, pendulous remaining breast, and upper abdomen (Fig. 6). This was the extent of the spread. Several days after the dermatitis reached its height, the itching and burning disappeared, leaving the patient quite comfortable. The reaction improved rapidly but occasional exacerbations occurred. Thirteen weeks after the onset, a few small patches of dermatitis

FIG. 6. Case IV. Taken one day after admission. The appearance of the dermatitis here is modified by the presence of a lotion. The angry look has somewhat subsided. The peripheral spread continued for about three more days.

were still present which occasionally would become reactivated. When the dermatitis had completely disappeared, the skin was left dry and indurated.

The burn continued to increase in size for a period of seven months; it then became an indolent ulcer (Fig. 7). To date there has been no evidence of healing.

Treatment first consisted of a silver protein preparation which was discontinued because of

FIG. 7. Case IV. The eczematoid dermatitis has subsided almost completely. The irradiation dermatitis, *A*, is covered with a black coagulum. The ulcer continued to increase in size to occupy almost the entire triangle, *B*, which represents the approximate size of the last portal of treatment.

aggravation of symptoms following its use. At intervals, olive oil, milk dressings and calamine lotion were used. The severe pain caused by the burn yielded to local refrigeration.

COMMENT

This infectious eczematoid dermatitis is seen about once in every 259 patients subjected to intensive roentgen irradiation, an incidence of 0.3 per cent. The onset of the dermatitis is from one to twelve or more weeks following the completion of irradiation, and the duration is about three weeks in abortive cases to several months in protracted cases. As a rule, the patients do not have the watery skin suggestive of an exudative diathesis, so frequently seen in seborrheic dermatitis.

Nearly always the first change noted is an increased reaction in the portals of treatment, followed by a peripheral, rather

symmetrical spread. The spread may be rapid, so as to cover half the thorax in less than a week, or it may be slow and limited to a relatively small area.

Characteristically, the rash is weeping and eczematoid, although in some instances the skin may be swollen, indurated and red for several days before vesiculation. In a few cases the reaction is branny. This branny reaction is seen in cases associated with draining lesions which have not received irradiation, such as Case 1 (see Fig. 1). Ordinarily the advancing edge is fairly distinct and in some cases so sharply demarcated as to resemble erysipelas. Occasionally, metastatic foci of dermatitis occur. These areas are less acute and usually subside before the primary areas.

The presence of a discharging ulcer or sinus is a common feature, although an exudative roentgen reaction may be the only antecedent factor. The dermatitis resolves more rapidly when not associated with a persistent discharging lesion.

In widespread cases, a mild febrile reaction may be noted. Eosinophilia has not been a feature. Drug hypersensitivity is not a factor; it was considered in studying the cases.

Curiously, most of the patients have been females. Early postoperative irradiation of mammary carcinoma with drainage from a portion of the surgical wound may be a factor. On the other hand, most of these cases do not develop the rash. I have seen the rash develop almost anywhere on the body.

In this clinic many cases of carcinoma of the skin are treated by electrosurgical excision followed by roentgen therapy, with a resultant discharging wound of six to eight weeks' duration. An unusual feature and difficult to explain is the almost complete absence of infectious eczematoid dermatitis as a complication of this mode of treatment. Nearly all such lesions are on the exposed parts of the body, such as the face. Their ready accessibility leads to more frequent dressing and therefore better care to the lesion and surrounding skin. The frequent removal of the accumulating discharge may account for the rare occurrence of the rash in these cases.

All patients who receive roentgen therapy in this clinic are routinely instructed on the first day of treatment as to the care of the skin. These instructions include the gentle application of olive oil or yellow petrolatum (colorless petrolatum is less cohesive) three, four or more times daily.

The treatment is empirical. Weak silver protein solutions have been a satisfactory form of treatment in some cases.

This dermatitis is not considered a contraindication to further roentgen therapy in cases of carcinoma, but treatment should be given with caution, as Bloch[3] reported a case of eczematous dermatitis which flared into an exfoliative dermatitis after roentgen irradiation of a uterine carcinoma.

The American literature is meager on the subject of spreading dermatitis associated with roentgen therapy. Most of the textbooks do not so much as mention reactions of this type. MacKee[19] briefly emphasizes this reaction as a complication of exudative or ulcerative irradiation reactions when he says, "Probably the most common and most annoying complication of exudative or ulcerative radiodermatitis is eczema of the infectious eczematoid dermatitis type."

In 1887, Unna,[35] the great German dermatologist, used the name seborrheic eczema and since that date many dermatologists have been snared by that captivating name.

Engman[9] separated a distinct type of dermatitis from the growing seborrheic eczema group. This he called infectious eczematoid dermatitis. Fordyce[11] emphasized the frequency with which various forms of generalized skin reactions are preceded by wounds or traumatisms which have become infected. Further, he emphasized the association of this history with so-called infectious eczematoid dermatitis (see Case 1, Fig. 1).

Whitfield,[37] according to Brown,[5] was the first to direct attention of dermatolo-

gists to the phenomenon of autosensitivity in its relation to skin affections. Whitfield was of the opinion that some of these generalized skin eruptions, following small, antecedent draining lesions, were a result of absorption of the patient's own broken-down products.

Brown says, "The evidence seems to prove that tissue damage is followed by autolysis and the production of a toxic substance or substances, which, absorbed into the general circulation, may determine pathological changes in the skin. . . . The focus of tissue drainage may be anywhere in the body: on the one hand, internal, deep-seated and difficult to determine; on the other hand, easily discovered on the surface of the skin."

Holzknecht,[14] in 1903, was probably the first to report a case of dermatitis apparently associated with roentgen therapy. He referred to his case as one of radiodermatitis bullosa resulting from an exudative reaction.

MacKee[2] was perhaps the first to offer an explanation of generalized reactions following roentgen irradiation. MacKee, who read Fordyce's paper, concludes that this skin eruption probably is an acute eczematoid dermatitis caused by sensitization of the patient's skin to his own discharges. Percival,[26] on the other hand, believes infection to be the cause and suggests the name follicular infective dermatitis. In cases which suffer from damaged skin and infection simultaneously, Whitfield, who advanced the theory of autosensitization, is not certain whether it is the products of tissue damage, bacterial toxins, or both that play a part in the etiology of the infectious eczematoid dermatitis. Some dermatologists and radiologists have been calling this complication acute seborrheic dermatitis. Dowling[7] reviews the various bacteriological aspects of seborrheic dermatitis and infers that the difference of opinion can be explained partly by the fact that not one but several different diseases are being included unwittingly by various investigators. Infectious eczematoid dermatitis frequently is included in the group. Whether infectious eczematoid dermatitis is caused by an infective agent, an autotoxin, or some other cause is not at present established. I believe, however, that many dermatologists now calling this condition seborrheic dermatitis will cease once their attention is called to the factors involved.

Percival[26] suggests the discarding of the name seborrheic dermatitis and the reclassification of the several diseases usually so diagnosed. He echoes the work of Engman in pointing out the existence of the entity of infectious eczematoid dermatitis. He also alludes to Fordyce's work in reviewing his experiences with infectious eczematoid dermatitis in Edinburgh. He states that, regardless of the looseness with which the term seborrheic dermatitis is used, infectious eczematoid dermatitis cannot be included in the group. He describes cases of infectious eczematoid dermatitis which appear following direct chemical or physical trauma, and cases which develop from antecedent isolated pustules or draining lesions. The first mentioned group apparently corresponds to the cases that develop in skin which is the site of an exudative or ulcerative roentgen-ray reaction only (see Cases II, III, and IV). The last mentioned group corresponds to the cases with discharging sinuses or ulcers per se (see Case I).

Case I was included in this paper because the infectious eczematoid dermatitis springing from an antecedent draining lesion should be well known. That it can and does arise from an exudative or ulcerative roentgen dermatitis should not then be strange. I agree that this dermatitis occurs as a direct complication of a roentgen skin reaction, as described by MacKee, but in some cases it may be coincidental with irradiation. A spreading dermatitis following roentgen therapy associated with an exudative or ulcerative skin reaction can be classified as a complication of the treatment. A case of spreading dermatitis associated with a discharging lesion in which the roentgen treatment has just

begun, or the dosage has not been sufficient to produce an exudative radiodermatitis, may be a coincidental complication resulting from the discharging sinus per se (see Case 11). Whether the roentgen ray acting on sensitized or damaged skin may be a precipitant factor in these cases is difficult to answer. That the roentgen rays and their effects on the skin are a contributory factor in these cases, however, seems likely.

Although the name infectious eczematoid dermatitis may be inadequate, I do not recommend a change until the entire group is reclassified as advised by Percival. The association of this dermatitis with roentgen irradiation calls for no overburdening of medical nomenclature, as trauma by physical agents already is recognized as one of the causes of infectious eczematoid dermatitis. The roentgen ray is the physical agent in these instances.

A physician who treats patients receiving roentgen therapy, and particularly one without the availability of a dermatological consultation, should be familiar with this type of reaction. This knowledge will enable the physician to advise his patient concerning the nature and probable course of the dermatitis, thereby gaining the patient's confidence and necessary cooperation.

REVIEW OF LITERATURE

Little has been written concerning universal skin reactions associated with roentgen irradiation. A review of the few contributions found is presented.

Exanthems and Roentgen Irradiation.* Although little has been written concerning skin reactions which occur outside the roentgen treated area, erysipeloid or scarlatiniform-like exanthem is the most vigorously discussed universal reaction associated with roentgen therapy. Holzknecht,[14] shortly after the advent of roentgenology, stated that roentgen exanthems, when they appear, always follow intensive roentgen therapy. Wetterer[36] estimated the incidence of this reaction at 1 to 100,000. He may well have said the reaction did not occur. Eczematoid dermatitis is not mentioned, except by MacKee.

Berenstein,[2] in discussing his experiences with generalized exanthems following roentgen irradiation, came to some startling and doubtful conclusions. Working almost exclusively with children, he found that 1.55 per cent of the treated cases developed an erythematous or scarlatiniform rash. Interestingly, nearly all of the patients were being treated for fungus diseases of the scalp. Berenstein suggested that the generalized rash was due to a specific effect of irradiation on the organism.

It is common knowledge among dermatologists that generalized eruptions of various types—erythematous, scarlatiniform or eczematous—are frequently seen with ringworm disease, scabies, etc., without irradiation. It is generally accepted that the so-called "ide" eruptions associated with ringworm infection are due to the toxic product of the fungus, and this probably explains many of Berenstein's cases, the roentgen therapy being purely coincidental.

Straus[32] in 1925 abruptly dismissed the subject of so-called roentgen exanthem by stating, "Roentgen exanthemata are rare and little understood." Reisner and Brada,[28] answering Berenstein's paper, state that they had not seen one case. They concluded that various reactions resembling scarlet fever, erysipelas or eczema could always be accounted for by allergy of medication or typical exanthems following tonsillitis, etc. It could always be proved, they felt, that a coincidental factor causes the dermatitis, not the roentgen therapy; in short, that exanthem due to roentgen irradiation does not occur.

Reisner and Brada are undoubtedly justified in emphasizing the importance of coincidental factors as the etiological factor in skin rashes associated with roentgen therapy; their premise, however, is too inclusive. Occasionally an infectious eczematoid dermatitis is a complication of roentgen irradiation. In my experience with roentgen irradiation in carcinoma, it ac-

* Term used herein refers to any generalized cutaneous eruption.

counts for most of the skin rashes spreading beyond the portals of treatment. So far as we know now the roentgen ray does not have any specific effect other than tissue irritation and eventual destruction. It must be understood, however, that from tissue damage rather profound effects may result. These effects vary naturally with the tissue concerned and are not yet completely understood. With damaged skin resulting in an exudative roentgen reaction, one of the requisite factors for an infectious eczematoid dermatitis is supplied. There can be little doubt that a type of infectious eczematoid dermatitis does occur occasionally; its occurrence should not provoke bewilderment but perplexing is its low incidence, when one considers that rather protracted exudative reactions following intensive roentgen irradiation for carcinoma are not rare.

The cases occasionally seen, such as Cases II, III and IV, are not due to allergy of medication, nor can they be explained as typical exanthems following tonsillitis, etc. It appears, therefore, that Reisner and Brada have not recognized the condition. I feel certain that some of the erysipelas-like reactions were identical with the cases I have described.

Pardo-Castelló[25] reports 4 cases of cutaneous eruptions which followed high voltage roentgen therapy. He refers to the eruptions as being allergic in nature but does not explain the basis for his opinion.

The most recent contribution which bears on the subject of exanthems associated with roentgen irradiation is that of Loewe and Camiel.[18] They report 4 cases of exanthems which developed following intensive roentgen irradiation for carcinoma in or about the mouth. The patients were forty-eight, sixty, seventy-five and seventy-eight years of age. All except the youngest had high fever, leukocytosis, and were critically ill. Two patients died; the youngest recovered after being only mildly indisposed. The patients in general had an intense roentgen reaction followed by changes in the skin spreading beyond the portals of treatment which required differentiation from erysipelas. A generalized erythematous reaction also appeared. The course was relatively protracted.

Loewe and Camiel conclude that perhaps they are dealing with a new clinical entity. They have considered other conditions and have excluded them. For example, cognizant of eczematoid dermatitis, they state that the reaction they describe bears no resemblance to it. They do, however, infer its resemblance to erysipelas. Loewe and Camiel further state that the roentgen rays are a factor, but other factors not yet known must play a part.

I cannot dismiss eczematoid dermatitis as lightly as do Loewe and Camiel as a possible diagnosis in their cases. It is perhaps true that eczematoid dermatitis is not usually associated with such violent constitutional symptoms as reported in 3 of the cases. It is likewise true, however, that occasionally elderly, constitutionally inadequate patients intensively treated for far advanced carcinoma of the pharynx or tongue develop severe constitutional symptoms with pyrexia, and sometimes die, as did 2 of their patients.

Drug Reactions Confused with "Roentgen Exanthem." It is true that in most instances rashes associated with roentgen therapy are in no way related to the treatment. Inasmuch as patients who suffer from carcinoma constitute the bulk of the radiologist's work, generalized skin rashes from drug or other hypersensitivity should always be considered when the etiological basis for the rash is not clear.

Uhlmann[34] reports a case in which a woman receiving roentgen therapy developed a severe generalized exanthem. The patient and family were advised by their family physician that the rash was due to a widespread roentgen reaction. Uhlmann, investigating the case, could not elicit a history of self-medication. The patient persistently denied that she had been using drugs. On a close search of the house, however, a box containing tablets of a barbiturate preparation was found. Only then did

the patient admit to self-medication and stated that she continued in this practice up to the moment of discovery.

In this case the roentgen reaction within the portals of treatment was much more severe than that usually seen with the same relatively small amount of irradiation. Uhlmann describes the intensity of the reaction as of the second degree type, coming on a few days after treatment. It appeared on all the portals at the same time—not progressively and successively. Uhlmann attributes this unusual reaction to a summation effect of the normal roentgen reaction superimposed on the drug reaction. This summation effect refers only to the intensified reaction within the portals of treatment, not to the universal reaction as apparently interpreted by Loewe and Camiel.

Uhlmann states that many physicians believe that a generalized exanthem can appear following intensive roentgen irradiation. He concludes that this is not true. In every instance of exanthem associated with roentgen therapy that he had seen, he was able to show to his satisfaction that the rash was merely coincidental with the treatment, and could be shown to be due to other causes. In his opinion, the only question open for discussion is whether the irritative effects may precipitate the skin changes if the diathesis is present.

It is to be remembered that patients frequently are taking drugs without the knowledge of the attending physician, and will refuse to admit taking drugs for various reasons, such as fear of embarrassing the family physician or fear of self-embarrassment because of taking drugs without advice. Another possibility suggested by Uhlmann is outright malingering. A rare patient may visualize a pot of gold in a court room following a malpractice suit.

I am certain that other experiences such as Uhlmann's have occurred, but have been unreported. Bromides, barbiturates, iodides, arsenicals and other drugs are well known as common causes of dermatitis medicamentosa. Because of the frequent use of drugs in patients subjected to roentgen therapy, allergy of medication should always be ruled out as a possible cause of skin rash. When called upon to treat a syphilitic with carcinoma, the policy of the Department of Radiology of this Clinic is to discontinue arsenical preparations and other drugs commonly employed in the treatment of syphilis. It is felt that these drugs increase the sensitivity of the tissues to irradiation. In other words, syphilis generally should not be actively treated when intensive roentgen irradiation is given.

Frazier and Hu,[12] working in China, described lesions of the skin due to vitamin A deficiency. This eruption is said to precede the xerophthalmia and hemeralopia, and is, in fact, frequently the first sign of the hypovitaminosis. From illustrations I have seen, this rash may in some phase closely resemble certain manifestations of dermatitis medicamentosa. The growing consciousness of hypovitaminosis in this country makes unlikely the possibility of seeing many examples such as those described by Frazier and Hu. I refer to it because in the roentgenologist's practice, he, as much as anyone, will encounter malnutrition and should be cognizant of this condition in order that he may not confuse it with dertitis medicamentosa, or other skin conditions.

A patient who develops unusual dermatological complaints during the course of roentgen treatment should be given as careful thought and study as any other patient who presents himself with a skin complaint. The fact that a patient is receiving roentgen therapy should not compromise the physician's attitude or interest.

Erysipelas Following Roentgen Irradiation. Kopari[16] reported a case of erysipelas following treatment with the roentgen rays. Our Case 11 was, for a short time, mistaken for erysipelas. If Kopari's case were a true case of erysipelas, it serves to emphasize the relative rarity of this disease associated with irradiation. Although it is conceivable that the irradiated skin with even a mild

roentgen dermatitis would supply fertile soil for the streptococcus of erysipelas or other organisms, erysipelas, nevertheless, is a rare complication of roentgen therapy. Indeed, roentgen therapy is frequently the treatment of choice in erysipelas. The roentgen therapy obviously has no specific effect, supplying only the means of entry for the organisms.

Herpes Zoster Following Roentgen Irradiation. A case of herpes zoster after irradiation was reported by Schreus[31] in 1926. In the same year, according to Schreus, another instance was reported by Groedel. The case reported by Schreus occurred in a child who had been treated for Hodgkin's disease. Both sides of the neck were involved and received roentgen therapy; the dosage was small. The herpes zoster occurred bilaterally thirty-seven days after the last treatment.

That herpes zoster is a rare concomitant of roentgen therapy is suggested by the lack of pertinent contributions in the literature. Schreus suggested that the herpes zoster might have been due to the specific effect of roentgen rays, but considered it unlikely because of its rare occurrence. He concluded that the virus of herpes zoster was present and the soil was rendered fertile by roentgen therapy. Langer[17] and others have shown that definite change in the vegetative nervous system can be produced with small doses. The rarity of bilateral herpes zoster suggests the possibility that the roentgen rays, in some way, may produce a "locus minoris resistentiae," thereby giving the virus already present abundant opportunities. Langer, who first became interested in the irradiation of the autonomic nervous system in 1921, reports no cases of herpes zoster or any other untoward effects in his review of many cases. Pancoast and Pendergrass[24] report herpes zoster as an occasional concomitant of Hodgkin's disease, apparently unrelated to roentgen therapy.

Herpes zoster also occurs not uncommonly as a complication of lymphogenous and myelogenous leukemia. Recently in this clinic 2 cases have been seen. The relative incidence of herpes zoster during roentgen irradiation in these cases has not been studied. It is probable that what has been said in the discussion of Hodgkin's disease and herpes zoster also applies in this group.

Skin Eruption Associated with Roentgen Irradiation of the Endocrine Glands. The most startling cases of skin rash associated with roentgen therapy were the 7 reported by Bray.[4] She described patients who developed a rash of uneven distribution following roentgen irradiation of the thyroid, breast, ovary and pituitary glands. Seven instances of this rash occurred in 136 patients treated. In describing the rash the author stated that the individual lesions consisted of smooth, edematous papules which appeared in groups and lasted about six days. Subsequent courses of roentgen therapy did not produce a recurrence. Because the rash failed to appear following later courses of treatment, Bray suggested the likelihood of a developed immunity to the effects of the roentgen rays. She further concluded that the irradiation had some specific effect on the endocrine glands, thereby producing a typical rash.

In studying the current literature, it is found that there is a mixed opinion concerning the relation of the endocrine glands to skin diseases. To cite the various opinions is beyond the scope of this paper.

Among radiologists working with hyperthyroid cases, it is well known that the skin of these patients is hypersensitive.[21] It is to be remembered that a widespread erythema is occasionally seen in hyperthyroidism. Various types of solid, patchy, grouped edematous areas and generalized pigmentary changes have been described, unassociated with roentgen therapy.[23] An increased incidence of skin infections simulating a type of acne vulgaris and due mostly to staphylococci is reported.[27] The large experience gained in irradiation of the thyroid gland does not mention cases such as Bray's.

Langer,[17] in his review of the literature,

largely German and Italian contributions, found many examples of cases treated over the hypophysis for menopausal symptoms, etc. In many cases the thyroid was also irradiated and no bad effects were noted. A series of 1,326 cases was treated over the hypophysis in Döderlein's clinic without resultant ill effects.

When roentgen irradiation of the pituitary gland is employed for the relief of menopausal symptoms, it should not be forgotten that divers skin changes may begin coincident with, and not as a result of, roentgen therapy. Schachter-Nancy[29] studied the affections of the skin common to the climacteric. He reviewed Maranon's[20] profound investigations into the changes and reaction of the skin during this period. Maranon pointed out that eczematous types of dermatoses may start for the first time during this period; that the onset of acne rosacea may be associated with the menopause, as may other skin diseases such as herpes zoster, melanoderma, etc. These possibilities should be remembered in skin changes associated with irradiation of women during the menopause. Countless cases in which the ovaries have been irradiated either inadvertently while treating carcinoma of the uterus, or intentionally in female castration have not shown the changes in the skin as reported by Bray.

A brief description of the salient features of Bray's cases should prove interesting.

Case I. *Marked Thyrotoxicosis.* This patient was given a total dosage of 1,200 r and 1,350 r of deep roentgen therapy to right and left lobes of the thyroid gland respectively. Following the treatment, smooth, solid, edematous, grouped papules appeared. The rash was found on the thighs, trunk and arms. It subsided in several days.

Case II. *Cystic Adenoma of the Thyroid Gland.* This patient, an adult woman, received 1,600 r deep roentgen irradiation, to each side of the neck. Some time following treatment the patient returned for a check-up and volunteered the information that she had had a slightly itchy, raised, red rash on the trunk and thighs. This rash lasted only a few days.

Case III. *Recurrent Carcinoma in a Mastectomy Scar.* One week following intensive roentgen therapy, a rash, which consisted of two patches of dusky red papules, one on the forearm and one on the abdomen, appeared overnight and subsided in a few days.

Case IV. *Recurrent Glands in Lower Right Abdomen.* This patient had a primary carcinoma of the left ovary removed surgically three and a half years before. For a recurrence the patient was given intensive deep roentgen therapy. Following treatment a firm, papular, edematous, itchy rash spread over the abdomen, upper arms and thighs. The rash disappeared in sixteen days and two months later the patient was dead.

Case V. *Carcinoma of the Cervix Uteri, Group III, Complicated by a Marked Thyrotoxicosis.* This patient was given deep roentgen therapy for the carcinoma of the cervix. In the fourth week of treatment, numerous discrete, red papules appeared scattered over the entire body. The rash subsided in six days. The thyroid gland was given roentgen therapy and the pelvis again irradiated without further appearance of the rash.

Case VI. *Recurrent Multilocular Cyst of the Ovary.* During deep roentgen therapy, a papular rash appeared and was scattered over the entire body. The individual lesions had a tendency to be grouped. The patient was not followed.

Case VII. *Hypergonadism.* A boy, aged twelve, was treated for hypergonadism by irradiation of the pituitary gland. More than three months following the treatment, the patient presented himself with his body thickly dotted with scratched papules and blood scabs, an intense weeping erythematous rash of the scrotum, a marked blepharitis, and dry, scaling hands.

Discussion of Bray's Cases. In studying these cases, one learns that dermatitis medicamentosa was not specifically eliminated as a possible factor in the development of the skin rash. The possibility of skin changes associated with thyrotoxicosis or the menopause was not considered. The scant eruption in Case I may have been made up of edematous nodules, occasionally seen in thyrotoxicosis. Case V could also be explained on a basis of thyrotoxicosis per se. Cases III and IV were probably not subjected to endocrine irradiation as the title of the paper suggests. Case III received treatment for a recurrent mammary carcinoma in the scar of an old mastectomy. At best it is doubtful whether the mammae are glands of internal secretion.[6] In this case the breast had been surgically removed previous to treatment. In Case IV the patient

received treatment for a recurrent ovarian carcinoma. The primary carcinoma had been surgically removed more than three years before. One can reasonably doubt that the rash in these cases constitutes effects from irradiation of endocrine glands. Case VII may have been an infectious eczematoid dermatitis. The weeping rash which appeared three months following roentgen therapy could hardly be the result of a specific effect of irradiation on an endocrine gland. Cases II and VI were not studied or followed adequately and therefore no conclusions can be drawn.

Bray states that cases such as hers have not previously been reported in the literature. I could find no comparable cases.

Although Kautzky[15] describes a case of skin eruption in hyperthyroidism which followed roentgen irradiation, I am not certain, however, that Kautzky considered sufficiently the possible cutaneous manifestations of hyperthyroidism per se. He concludes that the reaction is a summation effect, the factors being allergy plus a hypersensitive skin, fundamentally similar to the case described by Uhlmann. His case does not resemble those described by Bray.

Schreiner[30] reported a case of universal lichen ruber planus which became a universal exanthem twelve days following irradiation of the thyroid gland. The rash disappeared and later recurred following irradiation of the lumbar region. The recurrence indicates that irradiation of the gland had little to do with the rash.

In this clinic, on extremely rare occasions, universally distributed scarlatiniform eruptions have been seen following intrauterine radium therapy. Newcomet[22] believes this rash is probably toxic in nature as the patients run a toxic course with a febrile reaction and other constitutional symptoms. The noxious substance probably develops from the destruction of tissue. The rare occurrence of this toxic rash is perplexing, considering the many instances in which the lesion, the patient and the treatment are similar and comparable. This eruption does not suggest the cases described by Bray.

Turck's[33] theory that the variable reactions from toxic absorption are governed by the state of wellbeing of the animal is not accepted and certainly is not borne out in practice.

Enfield,[8] in 1937, reviewing the sequelae of roentgen therapy, mentions toxic erythema as an occasional complication of irradiation. He states that this reaction is seen about once in four or five years in a fairly active therapy practice. Enfield believes that the reaction is due to rapid destruction of radiosensitive tumor tissue with absorption.

Artz and Fuhs[1] believe that a toxic reaction associated with a rapidly fading scarlatiniform rash and pyrexia occurs and probably is the result of intoxication caused by the absorption of the products of cellular degeneration. They infer that the erythrodermia seen occasionally following roentgen therapy in cases of leukemia is explained by toxic absorption.

Epstein[10] reported a case of exanthema purpura following intensive irradiation of a carcinoma of the uterus. This suggests the rare cases seen by Newcomet.

Other Cases. Several references in the literature give accounts of the modification or conversion of skin affections, such as lichen planus, psoriasis, acne, etc., following roentgen irradiation.[13] As this paper is concerned only with reactions developing on apparently normal skin, these cases are not included in this review.

SUMMARY

Little has been written concerning exanthems which occur beyond the portals of treatment in association with roentgen therapy. Although some writers feel that exanthems which appear during or following roentgen therapy are merely coincidental, in my experience the majority of spreading dermatoses can be explained as infectious eczematoid dermatitis which develops as a complication of a localized exudative or ulcerative dermatitis produced by

the roentgen rays. I have presented first, as this should be well recognized, a case of eczematoid dermatitis which is the result of a chronic draining wound and which is in no way related to roentgen irradiation. I have then presented three cases associated with roentgen therapy and the fundamental similarity with the non-irradiated case is pointed out. The dermatitis is not the result of any specific effect of roentgen irradiation other than its power to damage tissue. The resultant exudative roentgen reaction produces, in some cases, an infectious eczematoid dermatitis, just as a persistent draining lesion of any origin may produce an infectious eczematoid dermatitis. The few contributions found in the literature concerning exanthems in association with roentgen therapy are also reviewed.

CONCLUSIONS

1. Those physicians concerned with the management of patients receiving roentgen irradiation will observe cases of dermatitis spreading beyond the limits of the portals of treatment.

2. In the experience of this clinic, the majority of skin eruptions spreading beyond the roentgen treated portals is best explained on a basis of infectious eczematoid dermatitis, although it is frequently diagnosed acute seborrheic dermatitis. Being cognizant of this condition will avoid bewilderment, as it not infrequently resembles erysipelas during the onset.

3. This dermatitis is an occasional complication of prolonged exudative or ulcerative roentgen reactions.

4. Infectious eczematoid dermatitis perhaps is not the best designation, but until the "seborrheic dermatitis—infectious eczematoid dermatitis" group is reclassified, there need be no further burdening of the terminology. The association of this reaction with roentgen therapy creates no demand for new terminology because physical trauma as a cause of infectious eczematoid dermatitis is known.

5. Whether infectious eczematoid dermatitis is actually on a basis of infection, as the name suggests, or is due to autosensitization is still being argued. Perhaps both are factors.

6. Infectious eczematoid dermatitis as a complication of an exudative roentgen reaction differs in no way at all from infectious eczematoid dermatitis which is known to occur occasionally in association with protracted draining lesions caused by chemical or physical trauma. The roentgen ray is the traumatizing agent which produces the necessary antecedent discharging lesion, namely, an exudative roentgen reaction, from which the infectious eczematoid dermatitis develops.

7. Erysipelas fortunately is a rare complication of roentgen irradiation.

8. Herpes zoster is a rare concomitant of roentgen irradiation. Its association with Hodgkin's disease and leukemia has been recognized.

9. In the light of present knowledge it appears unlikely that roentgen irradiation of the endocrine glands causes skin lesions which are due to a peculiar specific effect of the roentgen ray.

10. On rare occasions universally distributed scarlatiniform eruptions are seen following roentgen or radium irradiation of radiosensitive tumors.

11. Before writers attribute skin eruptions to a specific effect of the roentgen rays, first, they should exclude the possibility of allergic manifestations and particularly drug reactions; secondly, they should be familiar with the possible cutaneous manifestations of the disease under treatment; and thirdly, they should bear in mind that any skin disease may appear for the first time entirely by chance during a course of roentgen irradiation. If one follows this plan, only rarely will skin eruptions, other than infectious eczematoid dermatitis, be attributed to the effects of irradiation.

REFERENCES

1. Artz, L., and Fuhs, H. Roentgen Rays in Dermatology. William Wood & Co., Baltimore, 1937.

2. Berenstein, B. M. Generalisierte Exantheme nach Röntgenbestrahlung. *Röntgenpraxis*, 1932, *4*, 1014–1015.
3. Bloch, B. Universelle Dermatitis nach Bestrahlung eines Carc. uteri. *Schweiz. med. Wchnschr.*, 1925, *55*, 744.
4. Bray, S. Skin eruption caused by x-ray therapy on the endocrine glands. *Brit. J. Radiol.*, 1939, *12*, 312–315.
5. Brown, W. H. Some clinical manifestations of endogenous sensitization eruptions following local infection or injury. *Brit. J. Dermat.*, 1939, *51*, 197–207.
6. Cheatle, G. L., and Cutler, M. Tumours of the Breast. J. B. Lippincott Co., Philadelphia, pp. 36–37.
7. Dowling, G. B. Aetiology of seborrhoeic dermatitis. *Brit. J. Dermat.*, 1939, *51*, 1–7.
8. Enfield, C. D. Sequelae of roentgen therapy. *Kentucky M. J.*, 1937, *35*, 341–344.
9. Engman, M. J. Quoted by Schamberg, J. F. *J. Cutan. Dis.*, 1902, *20*, 102.
10. Epstein, P. Schwere, allgemeine Gefässchädigungen unter dem Bilde einer Werlhofschen Erkrankung nach lokaler Röntgen-Intensivbestrahlung. *Strahlentherapie*, 1925–1926, *21*, 416–418.
11. Fordyce, J. A. Infectious eczematoid dermatitis and possible influence of anaphylaxis in skin reactions. *J. Cutan. Dis.*, 1911, *29*, 129.
12. Frazier, C. N., and Hu, C. K. Cutaneous lesions associated with a deficiency in vitamin A in man. *Arch. Int. Med.*, 1931, *48*, 507–514.
13. Gouïn, J., and Bienvenue, A. Transformation de certaines réactions cutanées en lichen plan avec ou sans traitement radiothérapique. *Bull. Soc. franç. de dermat. et syph.*, 1927, *34*, 361–365.
14. Holzknecht, G. Fieberhafte Allgemeinerkrankung mit Exanthem bei Röntgendermatitis. *Arch. f. Dermat. u. Syph.*, 1903, *66*, 71.
15. Kautzky, A. Zur Frage der atypischen Hautreaktionen nach Röntgenbestrahlung. *Strahlentherapie*, 1937, *60*, 439–443.
16. Kopari, J. Roentgen therapy causing erysipelas with report of case. *Orvosi hetil.*, 1928, *72*, 438–440.
17. Langer, H. Roentgen treatment over vegetative nerve centers or ganglia in diseases presenting symptoms of disturbances of the vegetative nervous system. Am. J. Roentgenol. & Rad. Therapy, 1932, *28*, 747–763.
18. Loewe, L., and Camiel, M. R. Exanthem complicating neoplastic disease. Am. J. Roentgenol. & Rad. Therapy, 1940, *43*, 587–596.
19. MacKee, G. M. Roentgen ray reactions and injuries. In: Clinical Roentgen Therapy, E. A. Pohle, Editor. Lea & Febiger, Philadelphia, 1938, p. 745.
20. Maranon, G. Quoted by Schachter-Nancy, ref. 29.
21. Meyer, A. Sur la cause de l'hyper-radio-sensibilité cutanée des basedowiens. *Bull. et mém. Soc. de radiol. méd. de France*, 1937, *25*, 326–327.
22. Newcomet, W. S. Personal communication.
23. Osler, W. The Principles and Practice of Medicine. Tenth edition. D. Appleton & Co., New York, 1927, p. 900.
24. Pancoast, H. K., and Pendergrass, E. P. Occurrence of herpes zoster in Hodgkin's disease. *Am. J. M. Sc.*, 1924, *168*, 326–334.
25. Pardo-Castelló, V. Allergic cutaneous eruptions after high voltage roentgen therapy. *Arch. Dermat. & Syph.*, 1936, *33*, 886.
26. Percival, C. H. Aetiology of seborrhoeic dermatitis. *Brit. J. Dermat.*, 1939, *51*, 7–13.
27. Rienhoff, W. F., Jr. In: Practice of Surgery, by Dean Lewis. Vol. 6. W. F. Prior Co., Hagerstown, Md., 1936, Chap. 1, p. 106.
28. Reisner, A., and Brada, H. Generalisierte Exantheme durch Röntgenbestrahlung. *Röntgenpraxis*, 1933, *5*, 16–18.
29. Schachter-Nancy, M. Manifestations cutanées pseudo-érysipélateuses au cours de la ménopause féminine. *Rev. méd. de Nancy*, 1938, *66*, 425–426.
30. Schreiner, K. Rezidivierendes Röntgenexanthem. *Strahlentherapie*, 1923, *16*, 389–393.
31. Schreus, H. T. Herpes zoster nach Röntgenbestrahlung. *Dermat. Wchnschr.*, 1926, *83*, 1606–1608.
32. Straus. Quoted by Reisner and Brada, ref. 28.
33. Turck, F. B. The Action of the Living Cell. Macmillan Co., New York, 1933, pp. 139–166.
34. Uhlmann, E. Ueber eine durch Barbitursäurederivate ausgeloste Röntgenstrahlenreaktion. *Deutsche med. Wchnschr.*, 1936, *62*, 216–217.
35. Unna, P. G. Quoted by Claassen, H. Dermatitis seborrheica. *Ohio M. J.*, 1936, *32*, 1077–1081.
36. Wetterer. Quoted by Reisner and Brada, ref. 28.
37. Whitfield, A. Lumleian Lectures. *Lancet*, 1921, *2*, 122–123.

ROENTGEN RADIATION AS AN ANALGESIC AGENT*

By JOHN RUSSELL CARTY, M.D., *and* LUCILLE M. BOND, M.D.
NEW YORK, NEW YORK

CERTAIN aspects of the analgesic effect of roentgen irradiation on pain have been known from the earliest days of roentgen therapy. This effect has usually been considered as a secondary or side issue particularly in the treatment of cancer. It is proposed in this paper to discuss the use of roentgen radiation as an analgesic agent strictly from this standpoint, particularly with reference to the etiology, pathology and the results which may be expected from its use in painful conditions.

Severe and continuous pain is perhaps the most trying ordeal that a human being has to endure. Unremitting pain can quickly destroy the morale of the most robust individual. Not even the philosopher can endure the toothache patiently. The use of roentgen radiation as a purely analgesic agent has not perhaps been given the attention which it deserves. The thought has been rather confined to the correction of the underlying pathologic condition which caused the pain. While undoubtedly this has a great value, nevertheless roentgen radiation may at times be considered in the light of an analgesic agent without thought or hope, perhaps, of influencing the underlying pathologic condition, in the same manner that narcotics are usually given solely for the relief of pain and distress.

Pain may be caused by: (*a*) inflammation within the nervous structures themselves; (*b*) inflammation of structures in immediate vicinity of the nerves or nerve endings; (*c*) pressure of neighboring outside structures, including scar tissue, upon the nerves themselves; (*d*) infiltration of the nerve structures by tumor cells, and (*e*) irritation by trauma.

The action of roentgen rays on normal tissue is relatively poorly understood. Particularly is this true in the case of nervous tissue which has a highly complicated electro-physiological mechanism of its own. It has been well shown that large intensities of roentgen radiation applied directly to the brain is capable of causing cytolysis. This has been demonstrated using 200 kv. (peak) radiation by Elsberg, Davidoff and Dyke, and by Carty and Ray, who used low voltage radiation. We agree with the statement of Pohle who says, "From the fact that the nervous elements present a low radiosensitivity and do not show anatomical alterations, it does not follow that their function cannot be altered." The Arndt-Schultz Law of the German School postulates a stimulating, paralyzing and lethal action according to the amount of radiation given. It would not be profitable to pursue this rather theoretical discussion further. Suffice it to say that the action of roentgen radiation on inflammatory conditions, in a reduction of the size of tumors with consequent decreased pressure, and the action upon blood vessels serving nerves, is sufficient to account for, in large measure, the undoubted analgesic properties of roentgen radiation.

It is known by clinical experience that roentgen radiation, when properly administered, often has a beneficial effect upon inflammatory processes. There are many theories to account for this. Perhaps the most widely accepted one postulates a leukocytic destruction with liberation of antibacterial substances. It is probably true that there is little or no direct effect of the radiation upon bacteria themselves under conditions prevailing in the body. The anti-infectious quality of roentgen radiation would perhaps account for the cases whose etiology has an infectious basis. Also the action often produced by roentgen radiation in the relief of pain in malignant conditions, with one important exception to be mentioned later, can be explained on

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the basis of reduction in size of the tumor mass, thus relieving pressure.

There are several important considerations which must be borne in mind if we are justified in using roentgen therapy for analgesia: First, because of limitations inherent in the reaction of normal surrounding tissue, particularly skin, roentgen therapy cannot be used indefinitely. Now this very deficiency suggests that roentgen therapy, with some exceptions noted later, should be reserved for the more intractable cases where simpler forms of therapy have failed. Second, for obvious reasons it should not be used in cases where the pain might be caused by fibrosis with resulting pressure on the nervous structures. Finally, it must be borne in mind that roentgen radiation is a powerful agent and should be administered only by those well experienced in its use.

This study was based on 240 non-malignant cases where roentgen irradiation was given exclusively for pain. Thirty-seven cases of advanced cancer, which were treated solely for pain, were also included in the study. The non-malignant cases are divided as follows: 68 cases of arthritis and peri-arthritis, 73 cases of herpes zoster and 65 cases of radiculitis and neuritis. The acute inflammatory painful malignant conditions, excluding bursitis, were considered in another paper. The cases of herpes zoster were carefully studied in a separate report by McCombs, Tuggle and Guion, and painful malignant conditions were also given separate consideration. From all these studies certain fundamental considerations emerge, regardless of the etiological factor or factors causing the pain. These will now be discussed, leaving the details to the consideration of the appropriate etiological factor to be considered later.

(a) Age is important in estimating the probable analgesic effect of roentgen irradiation. Everything else being equal, a much better immediate and lasting relief will be obtained in a patient twenty years old than in one sixty.

(b) The sooner treatment is given in the course of the disease, the better the result will be.

(c) Exacerbation of the pain immediately following the first or second treatment is a favorable sign.

(d) Failure to obtain any relief during or immediately following an adequate series of treatments indicates that the treatment will not succeed and may actually do harm.

(e) An adequate amount of radiation must be given if satisfactory results are to be expected. This requires experience and thorough working knowledge of a given technique.

(f) Too large single doses may do harm, particularly if an infectious process is involved.

FUNDAMENTAL INDICATIONS FOR ROENTGEN THERAPY

In order that the use of roentgen therapy for the relief of pain should not be discredited, it is necessary to make a critical selection of cases in order that vague pains with a neurotic basis be excluded. These are as follows: (*a*) definite indication of pain such as lack of sleep, etc.; (*b*) localization of the pain in one general area; (*c*) local tenderness or sensory changes; (*d*) evidence of inflammation. In the long standing cases we prefer to treat only where other generally accepted methods have failed. Of course there are certain exceptions to this rule.

SUPERFICIAL INFECTIOUS CONDITIONS

The pain of a boil or carbuncle is familiar to all. This often can be materially reduced in intensity and duration by the use of roentgen irradiation. This is well illustrated where there is a deep-seated infection following intramuscular injections of medication into the buttocks. Usually the pain is decreased markedly and the duration often reduced by one-half. In our experience one of the first things the patient notices is a reduction of pain, followed later by either disappearance of the lesion, if treated soon enough, or early suppuration.

The pain of sinusitis in a certain number of cases can often be reduced materially.

This is probably because of a more efficient drainage although the amount or character of the discharge may not be materially altered. Roentgen irradiation should be reserved for stubborn cases where other methods, including surgery, have failed. Large single doses in infectious conditions are definitely contraindicated. The treatment of large areas in one sitting should also be avoided.

MALIGNANT CONDITIONS

The analgesic effect of roentgen irradiation in malignant conditions of course is familiar to all radiologists. However, I believe there is a tendency to withhold roentgen irradiation if there does not seem to be much chance of producing an effect on a tumor. In these circumstances the analgesic effect of roentgen irrradiation is sometimes lost sight of. However, it must be considered that there are certain instances where prolonged and exhaustive treatment seems to aggravate the pain, or more frequently not have any effect in this regard whatsover. A study of 10 such cases with autopsy findings showed that in 6 cases there was a definite infiltration of the nerve tissue with cancer cells. In the 4 remaining cases there was a great deal of fibrosis. The importance of fibrosis in the production of pain does not seem to be clear. Paradoxically, the pain of certain scars may be greatly relieved by roentgen treatment.

The use of roentgen therapy should not be withheld despite negative roentgenographic evidence, in instances where there is pain and the known course of the cancer would indicate possible metastasis in that region.

In general, a radiosensitive tumor that causes pain is more amenable to roentgen irradiation. However, the pain of a radioresistant tumor at times may be helped. This point should not be forgotten. This was emphasized in the case of a woman who had painful multiple myofibrolipomas. Roentgen irradiation was the only treatment to give relief.

HERPES ZOSTER

Roentgen therapy is an effective agent in the treatment of herpes zoster. Our results have been very satisfactory. The results have a definite relation to the interval between the appearance of the eruption and the time of roentgen treatment, and it has also been our experience that the results with the younger patients will be better than with the older group. It is absolutely essential to treat over the ganglia. Local treatment over the lesions alone is useless. However, I feel that in certain cases local treatment supplementing irradiation to the ganglia may be of help. This is particularly true in the herpes involving the face associated with severe eruption. McCombs, Tuggle and Guion have analyzed 73 cases of herpes treated by roentgen therapy. Their findings have confirmed our impression. Eighty-nine per cent of the cases treated within the first seven days after the appearance of the vesicles were cured, whereas after the fifteenth day this percentage dropped to 50. In favorable cases there may be an exacerbation of pain following the first few treatments. One should warn the patient about this. Relief is usually experienced after the second treatment. Insufficiently treated cases may recur; 1,000 to 1,200 r, measured in air, is generally necessary. The most unsatisfactory type of case to treat is that of the aged individual with a post-herpetic pain following herpes of a month or more previous.

The personal experience of one of us (J. R. C.) with roentgen irradiation is interesting and worth recounting. For two days severe shooting pains were experienced in the right upper jaw extending over the hard palate. Extraction of a questionable tooth gave no relief. In two days an eruption appeared on the hard palate typical of herpes. Roentgen irradiation was immediately applied to the sphenopalatine ganglion and locally in the afternoon. That night the pain which was severe became almost unbearable. Along towards morning

the pain eased. That afternoon the eruption started to become dry. The following day the pain disappeared, leaving a numb feeling. A total dose of 400 r was required. Because of the immediate application of roentgen irradiation results were most gratifying, and only a relatively small dose was required.

RADICULITIS, SCIATICA, CERVICAL NEURITIS

In general, the same remarks concerning herpes apply to the roentgen therapy of these conditions. However, we feel that it is quite important to treat the nerve trunks also. In sciatica and neuralgia the sacroiliac region is included. Again it is necessary to treat the ganglia, and a wide enough portal should be selected so that the radiation reaches the intervertebral foramina, as an inflammatory process in this region may be an important etiological factor in causing the pain.

Minor neuritic pains should not be treated by roentgen irradiation. There are many remedies which often give relief. A disregard of this warning will quickly bring the method into disrepute. Roentgen irradiation should be reserved for the severe resistant cases.

Our experience with roentgen irradiation in trigeminal neuralgia has been extremely limited. One case of the wife of a physician stands out. She has been free from pain for about three years since being treated. We give the irradiation locally as well as over the ganglion.

Three cases of syringomyelia associated with pain were treated. Our results were very unsatisfactory. In 2 instances the pain was definitely aggravated.

MYOSITIS, "LUMBAGO"

Good results have been obtained by roentgen therapy. Our experience is limited. The few patients treated have responded well. Overdosage must be carefully guarded against, particularly in the acute cases.

PAINFUL ARTHRITIS

Painful arthritic conditions may respond well to roentgen irradiation. Owing to the usually chronic nature of the disease roentgen irradiation should be reserved for severe cases where physiotherapeutic measures have failed. A good example of this is seen in one of our patients with coronary heart disease, who had a severely painful arthritis of the right shoulder. Various forms of heat had failed to give relief. Lack of sleep was having an adverse effect upon the cardiac condition. Following roentgen therapy the pain disappeared promptly and he remained without distress for about a year, when a second course of treatment was given. The patient died shortly after the second series from coronary occlusion.

Indiscriminate treating of all cases of painful arthritis will inevitably lead to discrediting of the method.

BURSITIS

Both the acute and chronic types respond well. In the latter instance we prefer to treat those cases which have not done well with physiotherapy. Relief may be gradual. It is a good idea to warn the patient that a certain amount of stiffness may remain, particularly if the condition has been of long standing.

ANGINAL PAIN

Good results following roentgen therapy of the parasympathetic ganglia for anginal pain have been reported by many observers. The frequency and intensity of the attacks are said to be diminished. We have not had sufficient experience to express an opinion.

TECHNIQUE

In most instances we prefer to use 200 kv. (peak) filtered with 1 to 2 mm. of copper plus 3 mm. of aluminum. Analgesia to a varying degree will usually be produced by a total dose of 100 to 1,200 r (measured in air) to the skin, depending upon the causative factor. In acute infections 100 to 200 r

may suffice. Herpes zoster and acute bursitis usually require 1,200 r. Until this amount of radiation has been given no case should be called a failure. Painful cancer obviously requires more radiation per area, usually 1,200 to 2,000 r, before results are obtained. These dosages merely serve as a guide. We feel that there is a tendency to undertreatment. In general, multiple small doses are much to be preferred to large single doses. Large single doses in the case of acute infection are definitely contraindicated and will probably do harm. With acute boils or other infections, more than 100 r should not be given per treatment, particularly during the first one or two treatments. Insufficient treatment may result in a satisfactory immediate result but there is a greater tendency to a subsequent recurrence. Burning, itching and tingling sensation may persist for several months following relief of pain. Patients showing this sign should be observed carefully as a recurrence seems very prone to take place.

Great care must be exercised to prevent the application of irritating drugs, hot water bags or other forms of heat over the treated area. Because the dosage may necessarily be high, a sensitization of the skin may result in a very severe reaction.

CONCLUSIONS

Roentgen radiation is a powerful and effective analgesic agent in many painful conditions. It should be used with discretion and only after much experience.

REFERENCES

1. Elsberg, C. A., Davidoff, L. M., and Dyke, C. G. Roentgen treatment of tumors of the brain in the operating room by direct radiation through the open wound. *Bull. Neurol. Inst. New York*, 1937, *6*, 19–32.

2. Carty, J. R., and Ray, B. S. Some experiences, experimental and clinical, with direct irradiation of neurological tumors during operation with low voltage radiation. *Radiology*, 1939, *32*, 325–331.

3. Carty, J. R. X-ray treatment of inflammatory conditions. *New York State J. Med.*, 1940, *40*, 106–109.

4. McCombs, P., Tuggle, A., and Guion, C. M. Roentgen ray therapy in treatment of herpe zoster. *Am. J. M. Sc.*, 1940, *200*, 803–808.

DISCUSSION

Dr. Frederick W. O'Brien, Boston. This paper is based on a study of 240 non-malignant cases but is rather general for it covers other types of cases. I think one should be certain of the mechanism and source of pain when one discusses pain associated with disease. If, for instance, one is dealing with a blocked ureter secondary to roentgen fibrosis or extension of cancer there is little reason to employ roentgen irradiation for relief of pain in such cases. The mechanism of pain in all benign conditions is not the same. It is certainly different in carbuncle than in herpes zoster and different in slipped disc than in localized arthritis deformans.

Perhaps many of you remember about two years ago Dr. Sosman read a paper on roentgen therapy in arthritis and in his characteristic fashion he treated half of the cases using a lead filter and half without and all did equally well. I think we have to be careful that our departments don't become psychotherapeutic clinics.

Dr. Carty (closing). Dr. O'Brien's remarks regarding the likelihood of treating neurotic patients is obviously important. However, if one selects these cases with care, and observes them very carefully, one will obtain the best results from the use of roentgen irradiation without discrediting the method. While a few of such cases may have crept into our series, the vast majority of the patients were suffering from severe pain, directly traceable to a definite pathological process.

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THE EXPERIMENTAL MODIFICATION OF THE SENSITIVITY OF YEAST TO ROENTGEN RAYS*†

By RUBERT S. ANDERSON *and* H. TURKOWITZ
Memorial Hospital
NEW YORK, NEW YORK

THE relative sensitivity of cells to ionizing radiations is obviously of great importance in therapy and in biological studies. The influence of physical variables, such as wave length, on the sensitivity of cells has received quite extensive study. Also many attempts have been made to modify the sensitivity of tumors in mammals by various methods. On the other hand, the influence on sensitivity of environmental factors acting directly on cell suspensions, which are free from the complicating interactions of an intact mammal, has received much less attention. Yet it is of importance to study conditions before, during and after irradiation which modify or do not modify the sensitivity of cells. If positive, such work might ultimately be an aid in therapy and in either case, an aid in understanding the character of the effects of ionizing radiations on cells.

It is generally agreed that when cells are irradiated with high energy radiation, such as roentgen rays, the effect is due to the ionization or excitation of molecules. Agreement stops there. From a chemical standpoint two general types of mechanism have been formulated for the biological effects which, it seems to us, suggest quite different approaches to the whole problem. First, the effective ionizations or excitations which occur during irradiation may occur directly in molecules that are absolutely essential to the cell. Or, second, the bulk of ionizations or excitations, which certainly occurs in the more abundant molecular species, water and proteins, may produce the biological result by reacting chemically with the essential molecules. The first type of mechanism has not apparently led to many attempts to modify cell sensitivity by experimental modification of the environment. The second type does lead to this sort of experimentation naturally. If one or more chemical reactions intervene between the first ionization and the irreversible damage it is reasonable to try to modify the chemical reaction and hence the biological result. Whatever the mechanism, ammonium hydroxide and carbon dioxide modify the inhibition of the division of fern spores (Zirkle) while ammonium hydroxide is a factor in the quantitative production of chromosome abnormalities, by roentgen rays (Marshak). Also oxygen has been found to be important in the relatively complicated cases of tumor fragments (Crabtree and Cramer) and seedlings (Mottram).

The immediate objective of the present work has been to study the influence of various conditions on the sensitivity to radiation of isolated cell suspensions. In the first phase of the work (Anderson) it was shown that the increase in time to the first cleavage produced in *Arbacia* eggs by roentgen rays is dependent to some extent on the presence of atmospheric oxygen during the irradiation. The behavior of a yeast *Torula cremoris* has now been studied in the presence and absence of atmospheric oxygen.

EXPERIMENTAL CONDITIONS

The cultures of *Torula cremoris* were grown in a medium of the following composition: 1 liter of distilled water, 2 gm. asparagin, 1 gm. ammonium sulfate, 1.5 gm. potassium dihydrogen phosphate, 0.125 gm. magnesium sulfate, 0.125 gm. calcium

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chloride, 32 gm. Mead's dextri-maltose,* 2 gm. peptone.† Solid media had in addition 23 gm. of Difco bactonutrient agar per liter. In order to have reasonably constant amounts of seeding in cultures for experiments, the cells from a slant were suspended in liquid medium in an ordinary pyrex 25 ml. culture tube and the transmission read in a nephelometer. The light source was a 6 volt automobile light unfiltered and the intensity was measured with a photronic cell. A 50 or 70 ml. volume of medium in a 100 ml. bottle was then seeded with the equivalent of 1 ml. of a suspension having 96 per cent transmission.

The radiation was from two water-cooled roentgen tubes operated at 30 ma., 190,000 volt (peak), and was unfiltered except for the heavy glass wall of the roentgen tubes and the glass of the Thunberg tubes. The suspensions were irradiated 30 cm. from each target at an intensity of 690 r per minute.

* *Torula* does not form acid from maltose but apparently the dextri-maltose product contains necessary growth substances. The medium was one previously used in this laboratory and it has been retained for this work to avoid the introduction of additional variables.

† Omitted in the later experiments.

EXPERIMENTAL RESULTS

As pointed out many years ago by Lacassagne, even a single cell may have different "sensitivities" to radiation depending on the particular criterion chosen as a measure of the radiation effect. The criterion of radiation effect chosen for this work has been the capacity of the cell to produce a visible colony within two or three days after plating. An injured cell may produce a small colony of a number of daughter cells after irradiation, as shown earlier by Henshaw for *Saccharomyces*, and the cells of this colony may continue intact for at least several days and perhaps longer. It does not produce a colony visible without magnification within that time and counts made over a period of several days are essentially constant. There is, of course, good reason to believe that all of the cells which have this one factor in common

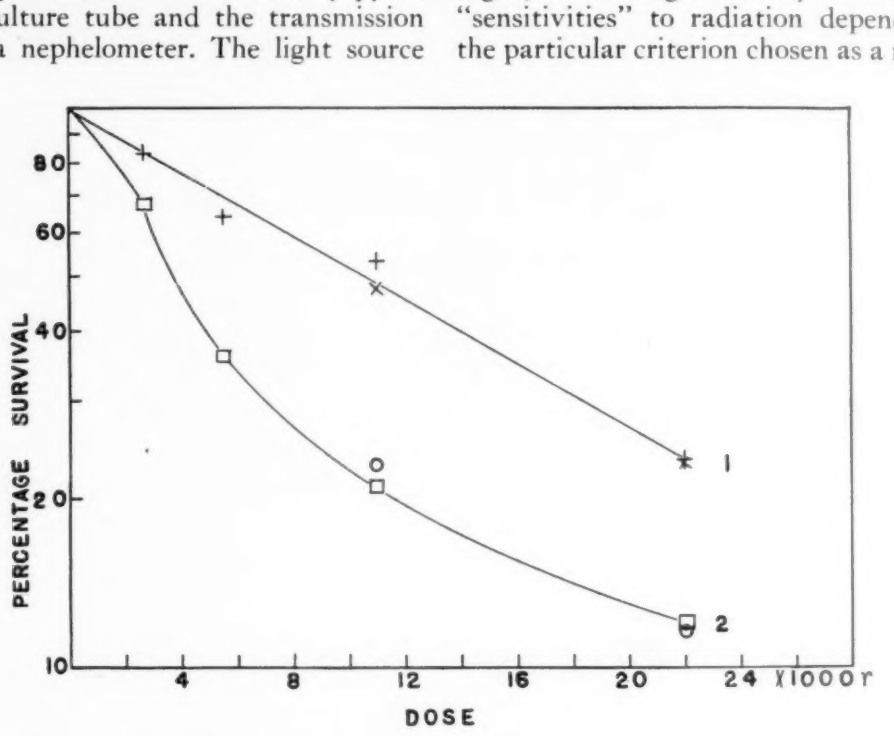

Fig. 1. Cultures were from seventeen and a half to eighteen and a half hours old except for the experiments represented by the symbols *o* and *x* which are from a separate series using twenty-four to twenty-seven hour cultures. The cultures were unstirred during the growth period in both series.

do not receive the same kind of injury.

For the first experiments, which compare the sensitivity of cell suspensions irradiated in the presence and absence of atmospheric oxygen, a mother culture grown in a liquid medium was distributed among six Thunberg tubes, 3 ml. in each. These were all thoroughly deaerated by means of alternate evacuation and filling with hydrogen freed of oxygen by passing over hot, platinized asbestos. The suspensions stood from five to twenty minutes in the deaerated conditions and then half of them were again saturated with air. Two tubes from those still deaerated and two which had been resaturated with air were irradiated immediately. After irradiation all were opened to air, convenient dilutions made through successive bottles of distilled H_2O* and 1 ml. plated on agar plates in the usual way. The different samples were, therefore, handled as nearly identically as possible except during the forty to fifty minutes immediately preceding and during the irradiation.

As shown in Figure 1, a markedly smaller sensitivity is observed in seventeen to twenty-four hour unstirred cultures free of oxygen, curve 1, than in cultures saturated with atmospheric oxygen, curve 2. For 50 per cent survival, in these particular examples, two or three times as much radiation is required in the absence of air as in its presence. It may be significant that the effect is in the same direction as found by Crabtree and Cramer and by Mottram using entirely different tissues and criteria. Since it is the comparison of sensitivity that is of major interest, the data for corresponding points with and without oxygen were obtained at the same time and are therefore strictly comparable. For any other purpose than this comparison the data must be used with caution. Little attention has been given to determining the absolute values or the exact forms of the curves and these are probably influenced by the presence of some double cells. Although curve 1 has been drawn as a straight line, the deviations from it may be real. Nor for the present is any particular significance attached to the "S" shape given to curve 2. The one additional inference to be drawn now is that the data for this *one type of culture* irradiated in the presence and absence of oxygen cannot be plausibly represented by two similar curves because of the positions of the points at 11,000 r and 22,000 r with respect to the origin.*

The half survival value, in air about 4,000 r using the described criterion, is very much lower than that reported for other yeasts by Lacassagne, Glocker, Wyckoff, and Henshaw. For the earlier work this seems to be in large part a matter of the criterion used and will be discussed more fully in a later report. Under these particular conditions, *Torula cremoris* compares in sensitivity with the values reported for bacteria.

The same experiment was then tried in another way. When a culture grows in an unstirred test tube for sixteen to eighteen hours an oxygen lack is produced and it seemed that this might be enough to influence the sensitivity. To test this a series of cultures were grown in 25 ml. tubes, each containing 13 ml. of medium. After about seventeen hours' incubation, half of them were aerated by shaking vigorously and both the shaken and the unshaken cultures were irradiated immediately.

As shown in Table I the same general type of data is obtained as when oxygen is removed artificially. For 50 per cent survival the figures are about 4,000 r compared to 14,000 r for the stirred and unstirred cultures respectively. The differences in the distribution of the cells within the stirred and unstirred cultures necessarily introduced some difference in the average dose given to the cells in the two experi-

* A comparison of counts using distilled H_2O and medium for dilution were the same within error.

Irradiation	Dilution by Water	Medium
0 r	100%	105%
11,000 r	21	22
22,000 r	9	8

* The few values given for slant cells in Table II do not suggest the same difference in this case.

ments. The cells were not only under a different average thickness of water but the relation of many cells to the two targets was not the same. However the 50 per cent survival dose in the unstirred culture is certainly two or three fold greater than in the stirred culture.

TABLE I

Dosage	Percentage Survival	
	Tubes Shaken	Tubes Unshaken
2,750 r	85	95
5,500 r	41	79
11,000 r	19	71
22,000 r	11	35

It is reasonable to suppose that oxygen accounts for much of the observed difference between the stirred and unstirred cultures. However, changes in the local concentrations of metabolic products and other components of the medium occur and these also may influence the result.

The first type of experiment, that is removing the oxygen artificially, has been extended to cultures prepared in other ways and the data are given in Table II. An effect of oxygen removal is shown in six to eight hour cultures and in suspensions of cells from six or seven day old slants. The former culture was growing rapidly, the latter was at most just beginning to grow.

That the oxygen effect may be modified sharply and requires further examination is shown by one series of experiments in Table II. Twenty-four hour cultures that had been sampled and hence shaken once or twice during the previous few hours showed a much smaller oxygen effect than the other cultures. Since these conditions are obviously complicated, the reason for this difference cannot be given.

DISCUSSION

The most common source of error in this type of experiment using plate counts is a difference in the aggregation of the cells at the time of plating. If cells of identical sensitivity occur singly in one case when plated and as pairs in another they will show apparent differences in sensitivity to radiation. This is of course apart from any modification of the individual response of each produced by the presence of the other. For the comparison of survivals in the presence and absence of oxygen to be valid, it is therefore necessary to show that the state of aggregation of the cells when plated was the same in the two cases. This is desirable irrespective of whether or not they occurred initially as single cells.* Actual counts showed about the same distribution of single and budded or double cells in the two cases. More convincing evi-

TABLE II

Dosage	$4\frac{1}{2}$–$7\frac{1}{2}$ hr. Cultures		Percentage Survival			
			Suspensions of Cells from 6–7 Day Old Slants		22–24 hr. Cultures Previously Shaken	
	In Air	Air Free	In Air	Air Free	In Air	Air Free
5,500 r			43	62		
11,000 r	40	65	10	43	47	55
22,000 r	29	45	1	20	20	28

* Actually the proportion of single cells varied a great dea depending upon the method used for preparing the culture. As mentioned, the presence of double cells would be expected to modify the form of the dose-survival relationship and the lack of constancy in different types of cultures makes the comparison of their sensitivities difficult. This is not relevant to the comparison of survivals in the presence and absence of oxygen and will be discussed in a later report.

dence is furnished by a comparison of the controls for the suspensions irradiated in air and for those irradiated in the absence of air. If the average of the former is set at 100 the latter is 101 ± 5. This shows that the state of aggregation must have been essentially the same in the two cases. The possibility remained that although the control tubes remained the same, one effect of the irradiation itself was to change the state of aggregation of the cells. A microscopic count of the number of units immediately after irradiation gave:

Control	193
22,000 r in air	217
22,000 r without air	210

These show no difference that needs to be considered.

Nothing is known as yet regarding the mechanism of the oxygen effect. At present it is idle to speculate as to whether the oxygen produces the change by rapidly modifying some system within the cell so that the cell becomes more "sensitive" or whether oxygen reacts as it does in photodynamic action. The data do not give any specific evidence for or against either of the theories mentioned initially but they are the kind of result to be expected from the second mechanism.

In conclusion, then, it can be said that the presence of oxygen at the time of irradiation increases the sensitivity to roentgen rays of *Torula cremoris* when the survival has been measured as described and the cultures have been grown under several of the above conditions. The results are being extended to see if the effect is more general. Also the reason for the non-appearance of the effect on *Torula* under some conditions is being examined.

SUMMARY

Torula cremoris cells grown under several conditions are more sensitive to roentgen rays in the presence of oxygen than in its absence.

We are indebted to all the members of the Physics Department, Drs. Failla, Folsom, Marinelli, Quimby and White, for assistance on the physical characteristics of roentgen rays and roentgen-ray equipment and to Dr. Henshaw for helpful discussions which served as a general introduction to the study of biological radiation effects. We are also grateful to the National Cancer Institute for a grant.

REFERENCES

1. Anderson, R. S. The x-ray effect on the cleavage time of Arbacia eggs in the absence of oxygen. *Biol. Bull.*, 1939, *77*, 325.
2. Crabtree, H. G., and Cramer, W. Some factors determining the susceptibility of cancer cells to radium. *Proc. Roy. Soc., B.*, 1934, *113*, 238.
3. Glocker, R., Langendorff, H., and Reuss, A. Ueber die Wirkung von Röntgenstrahlen verschiedenen Wellenlänge auf biologische Objekte. *Strahlentherapie*, 1933, *46*, 517–528.
4. Henshaw, P. S., and Turkowitz, H. Some effects of roentgen rays on *Saccharomyces cerevisiae*. Am. J. Roentgenol. & Rad. Therapy, 1940, *43*, 93–106.
5. Lacassagne, A. Difference de l'action biologique provoquée dans les levures par diverses radiations. *Compt. rend. Acad. d. sc.*, 1930, *190*, 524–526.
6. Marshak, A. Alteration of chromosome sensitivity to x-rays with NH_4OH. *Proc. Soc. Exper. Biol. & Med.*, 1938, *38*, 705–713.
7. Marshak, A. Stage of mitosis at which chromosomes are rendered less sensitive to x-rays by ammonia. *Proc. Soc. Exper. Biol. & Med.*, 1938, *39*, 194–198.
8. Mottram, J. C. On the alteration in sensitivity of cells towards radiation produced by cold and by anaerobiosis. *Brit. J. Radiol.*, 1935, *8*, 32–39.
9. Wyckoff, R. W. G., and Luyet, B. J. Effects of x-rays, cathode, and ultra-violet rays on yeast. *Radiology*, 1931, *17*, 1171–1175.
10. Zirkle, R. E. Modification of radiosensitivity by means of readily penetrating acids and bases. Am. J. Roentgenol. & Rad. Therapy, 1936, *35*, 230–237.

DISCUSSION

Dr. Ashley W. Oughterson, New Haven, Conn. I appreciate being asked to discuss this paper, particularly since I am not a roentgenologist. I am, however, interested in the problems of cancer therapy.

Dr. Anderson has pointed out the importance of determining how the biological effects of roentgen rays may be modified. He has stated that this is of importance not only in the interpretation of the variable results of therapy but also in the hope that therapy may thereby be made more effective. Observations such as he

has reported may therefore be fundamental and essential to a better understanding of how roentgen irradiation cures cancer.

The changes produced in cells by roentgen rays or radium and the reasons why tumors disappear or regress are not well understood. The possible differential effect of wave length and dosage has received much attention. The limitations of improving results by varying wave length and dosage are becoming increasingly apparent.

The possibilities of changing the chemistry of the cell or the environment in which they live have been by no means exhausted. Clinical experience strongly suggests that the condition of the cell or the host in which it lives may determine the response obtained following radiation therapy.

A knowledge of how such changes may influence the effects of roentgen rays or radium is therefore indispensable.

Studies on unicellular organisms as reported by Dr. Anderson are of great assistance in determining what may happen in more complex structures such as tumors in animals. His work confirms some of the observations of Cramer, Crabtree and others who have worked with mammalian tumors in tissue culture.

While it is theoretically possible to consider the reaction of the isolated cell, nevertheless from the practical viewpoint of the radiation therapist, the cell cannot be isolated from its environment.

Furthermore, from the standpoint of interpreting results in man, it is important to determine whether these changes induced within the cell or its environment are within the limits obtaining in tumors or normal tissues of man. This is particularly true if these methods are to be used in further improving radiation therapy by influencing the cell or its environment.

Vol. 46, No. 4

NON-HARMFUL EFFECTS OF IRRADIATION OF THE PITUITARY REGION OF RABBITS*

By J. KOTZ, M.D., F.A.C.S., JOSEPH F. ELWARD, M.D., *and* ELIZABETH PARKER, M.A., M.D.

THE last ten years have seen the development of intensive research on the physiology of the reproductive cycle in the female which has done much to elucidate the endocrine mechanism of this process. From this has followed a better understanding of the disturbed physiology underlying the functional disorders of menstruation. The ovarian hormones in crystalline form and potent gonadotropic substances have been available for clinical use for the past several years. We had hoped that the addition of these substances to our armamentarium, together with the better understanding of the pathological physiology of the condition, would render therapy of the functional menstrual disorders simple and effective. Such has not been the case. The majority of these disorders are not corrected by organotherapy alone. At best, they can sometimes be controlled or improved. To be cured, the endocrine balance, which has been upset, must be returned to normal. We have therefore sought other means of effective therapy. Irradiation of the pituitary seems to offer some hope of solution of this problem.

At the International Congress of Radiology in Chicago in 1937, we reported our results with the use of irradiation of the pituitary gland in functional disorders of the female. Since the publication of this work,[1] the questions have been repeatedly asked: Is the use of irradiation harmful, and is there any danger connected with such a procedure? To answer these questions the study here presented was undertaken.

From a clinical standpoint, no demonstrable harmful results have been produced by the use of irradiation. The patient sometimes complains of a slight headache or nausea and dizziness on the day of treatment but this passes very quickly. In the first cases treated, epilation occasionally occurred at the site of treatment, but this has been avoided by the adjustment of dosage. No physiological signs have developed after treatment to indicate disturbances of pituitary function or neurological signs to indicate injury to the surrounding brain tissue. Many of the patients so treated have conceived and been delivered of normal children. The time which has elapsed since treatment, even in the earliest cases, now eight years, is too short to say that remote after-effects do not occur, but judging by their present condition, there seems to be no reason to expect that there will be late evidence of injury.

From the experimental standpoint, there have been many reports of the effect of irradiation on the pituitary gland and its consequential effects on other glands of internal secretion in various laboratory animals. The results have been quite variable due mostly, we believe, to the marked variation in dosage.

Lawrence, Nelson and Wilson[2] irradiated albino female rats thirty to forty days old. Under amytal anesthesia, the pituitary regions were exposed to filtered radiation as follows: 180 kv., 25 ma., 0.5 mm. Cu and 1 mm. Al filters, distance 50 cm., giving 52 r per minute through an opening 1 cm. in diameter over the dorsum of the head, the rest of the body being shielded with lead. The total dosage, 1,040 r, is an excessive dose as compared with that used in the human. They noted a temporary decrease in the rate of growth of the animals. Histological examination of the pituitary glands consistently revealed characteristic changes which presumably accounted for the retardation of growth, the inhibition of ovarian function and the atrophic condition of the thyroid and adrenal glands. The immediate period of suppression was followed

* From the George Washington University School of Medicine Endocrine Clinic and Department of Radiology.

by a gradual recovery of the pituitary and consequently of the organs influenced by its hormones. From these findings it was concluded that though the pituitary gland of the young albino rat is relatively radioresistant, nevertheless it can be influenced by irradiation. No definite clinical implications were drawn but the experiments seemed to suggest that the non-adenomatous human pituitary gland can be influenced by therapeutic doses of roentgen rays.

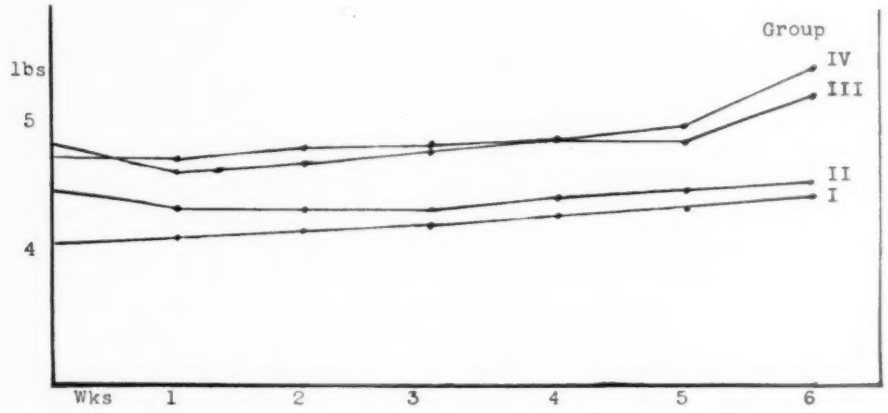

Chart I. Average weight of rabbits after being treated by irradiation of the pituitary region.

Hartman and Smith[3] irradiated the pituitary glands of 13 sterile female monkeys using the following factors: 200 kv., 20 ma., 50 cm. distance, size of fields 4×5 cm., 0.5 mm. Cu and 1 mm. Al filters, the only variable was dosage, 60 to 400 r being used. Of the 13 animals which were not ovulating, only one ovulated after the treatment which they thought might well have been due to chance. However, one-third of the monkeys resumed the ovulatory function and conceived at the next breeding season. They therefore concluded that while there were no demonstrable beneficial effects, irradiation was not harmful.

METHOD

Twenty adult female rabbits, under light nembutal anesthesia, were treated with varying amounts of radiation in the region of the pituitary gland, killed at varying intervals and the pituitary, ovary, thyroid and adrenals examined for the purpose of determining whether there was any evidence of histological changes in these organs which might be attributed to the effects of irradiation.

The factors of irradiation in all cases were: 200 kv., 25 ma., 50 cm. distance, and 0.5 mm. Cu and 1 mm. Al filters. The rabbits were divided into four groups, Group I receiving 201 r delivered in five and a half minutes; Group II, 300.3 r in eight and a quarter minutes; Group III, 400.4 r in eleven minutes and Group IV, 509.6 r in fourteen minutes. Only one treatment was given each animal. The factors used in the human are the same, with 100 to 130 r being given in five to six minutes at one to three week intervals for four treatments. These animals received tremendous doses of roentgen rays in comparison to the therapeutic doses given humans when relative weights are considered.

Five control animals constituting Group V were subjected to the anesthesia, but no irradiation was given. All animals were then returned to their usual environment and observed for any abnormality of behavior, and weighed at weekly intervals. One animal from each group was killed on the third, fourth, fifth, sixth and seventh week after the treatment.

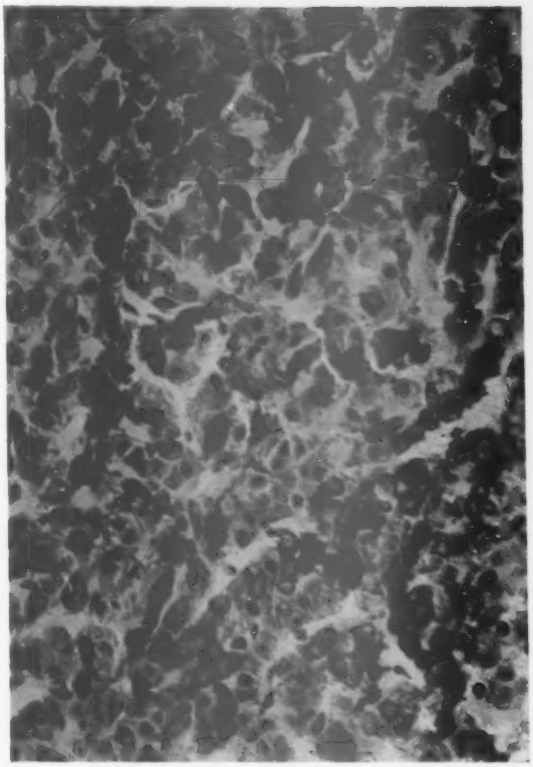

Fig. 2. Pituitary (×600). Animal Group IV killed three weeks after irradiation.

The tissues were fixed by perfusion through the heart of the anesthetized animal of Helly's fluid according to the technique of Shay.[4] The pituitary gland tissue was stained by the Heidenhain's modification of Mallory's stain as described by Dawson and Friedgood.[5] The ovaries, thyroid and adrenals were stained with hematoxylin-eosin.

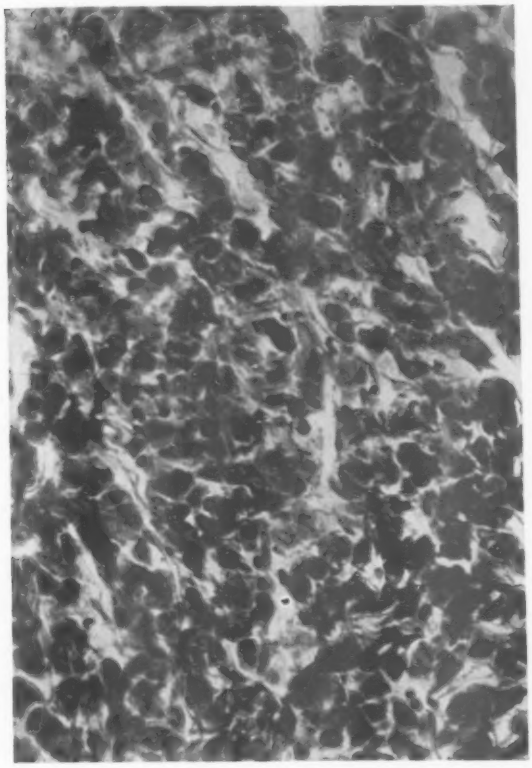

Fig. 1. Pituitary (×600). Control animal.

RESULTS

The average weight changes in each group are represented in Chart 1. The animals after treatment showed no diminution in activity. They all ate well and retained their weight.

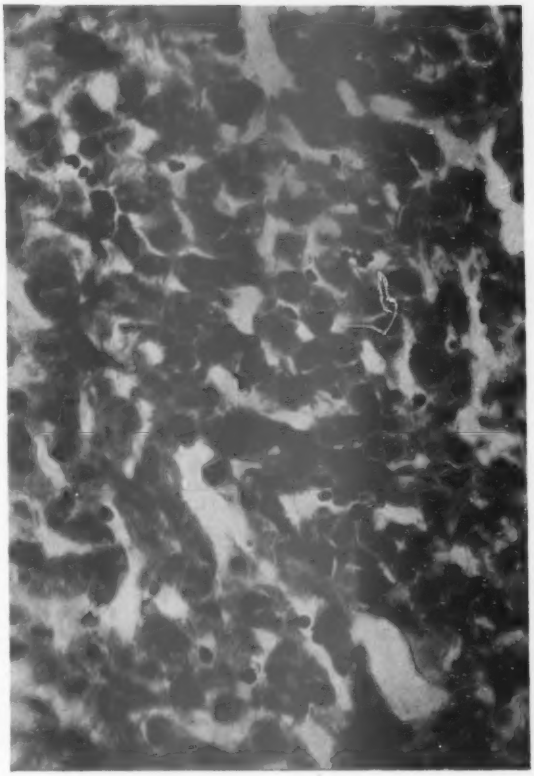

Fig. 3. Pituitary (×600). Animal Group IV killed six weeks after irradiation.

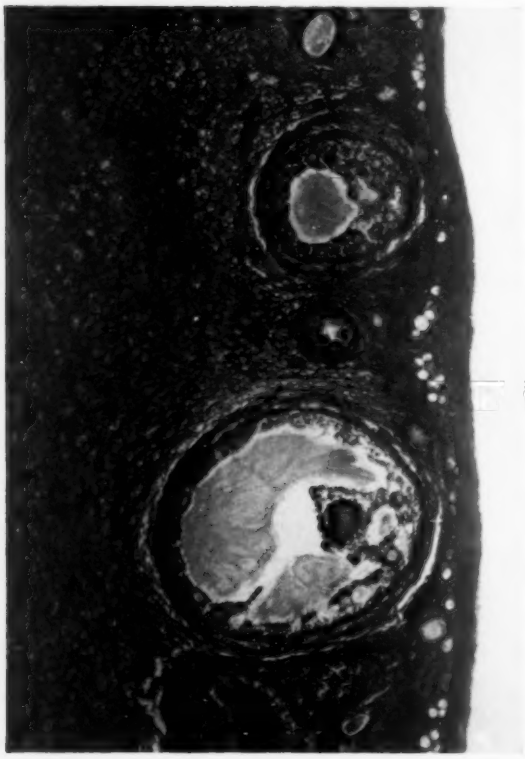

Fig. 4. Ovary (×80). Control.

Pituitary. There was no demonstrable change in the size or structure of this gland in any of the rabbits. The normal ratio of the acidophil, basophil and chromophore cells of the anterior lobe was maintained. The cells were apparently all in good condition, there being no evidence of degeneration. Typical sections taken from the surface of the mid-dorsal region are shown in Figures 1, 2 and 3.

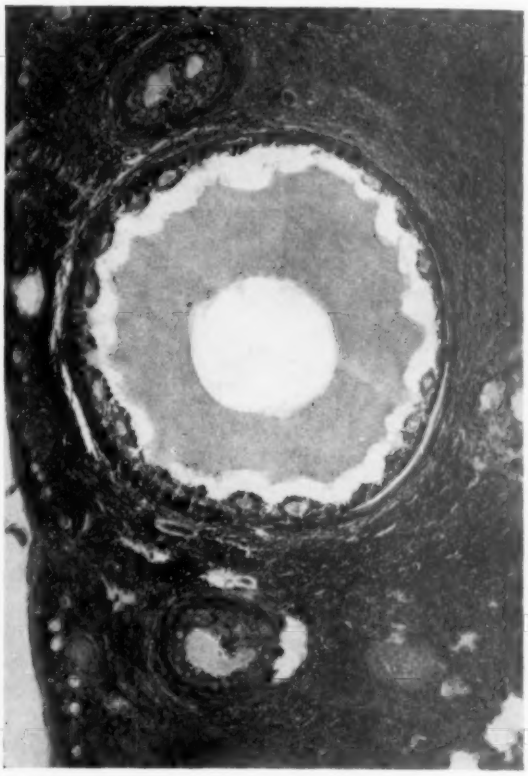

Fig. 6. Ovary (×80). Animal Group IV killed at six weeks after irradiation.

Ovaries. There was no change in the size of the ovaries with variation in amount of radiation or with the time which was allowed to elapse after the treatment before

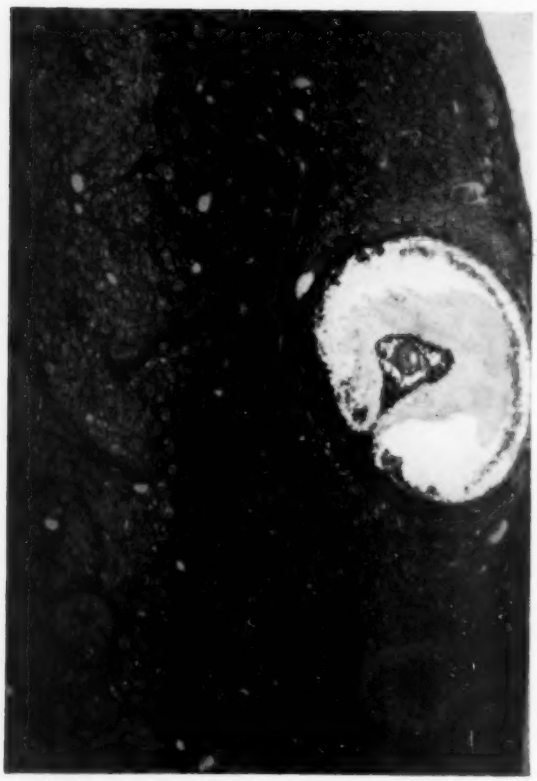

Fig. 5. Ovary (×80). Animal Group IV killed at three weeks after irradiation.

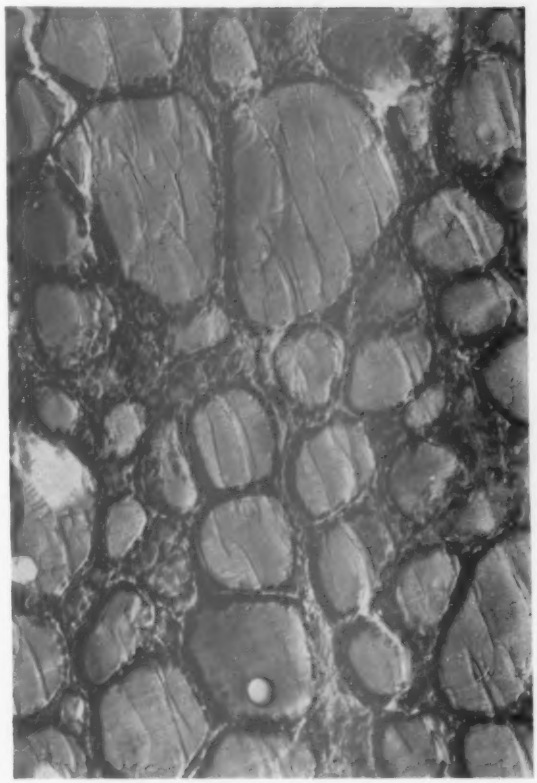

Fig. 8. Thyroid (×280). Animal Group IV killed three weeks after irradiation.

the animals were killed. Figures 4, 5 and 6 represent typical sections of ovaries of the control and treated animals. The number of primordial follicles were within the normal limits of variation and were well pre-

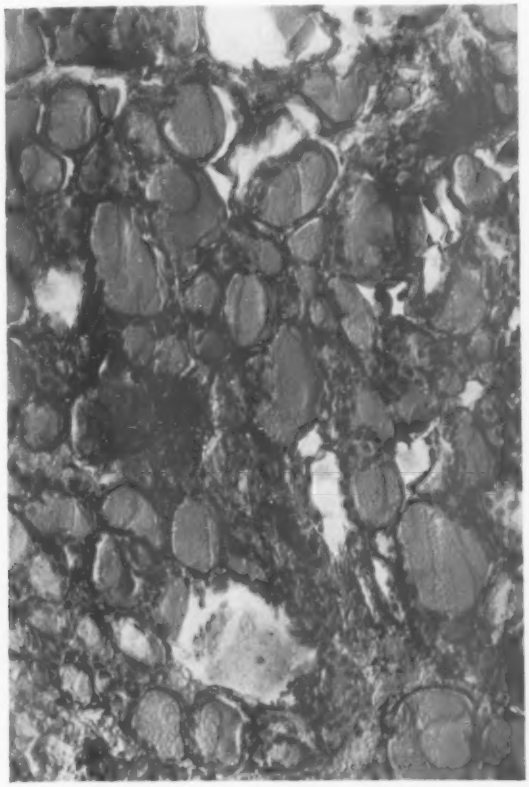

Fig. 7. Thyroid (×280). Control.

served throughout the series. There was no variation in the number of mature follicles from that of normal. There was no evidence of ovulation or of corpus luteum formation. In the ovaries of the animals receiving the larger doses of radiation, there seemed to be a tendency to cyst formation since the follicles were somewhat larger and contained more fluid than those of the control

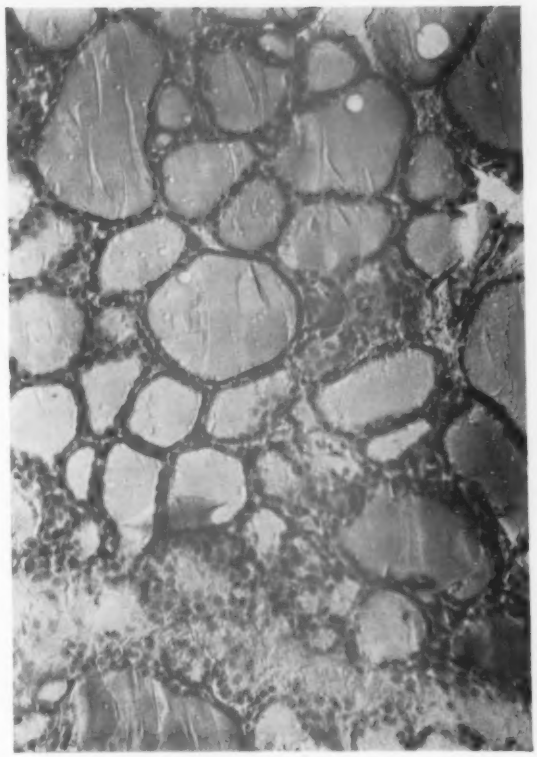

Fig. 9. Thyroid (×280). Animal Group IV killed six weeks after irradiation.

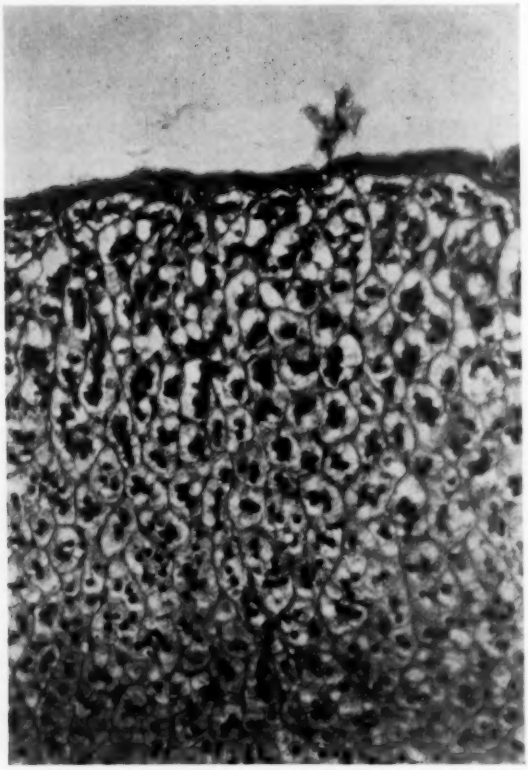

Fig. 10. Adrenal cortex (×280). Control.

animals. In some there was a moderate leukocytic infiltration which occurs with ovulation.

While this demonstrates that there was no deleterious effect on the ovaries, we do not believe that it demonstrates that roentgen irradiation has no effect on the ovarian cycle in humans. There is a marked species difference between the human and the rabbit. In the human there is a regular, recurring cycle of maturation, ovulation and corpus luteum formation, while in the rabbit many mature follicles may be present in the ovary at one time but ovula-

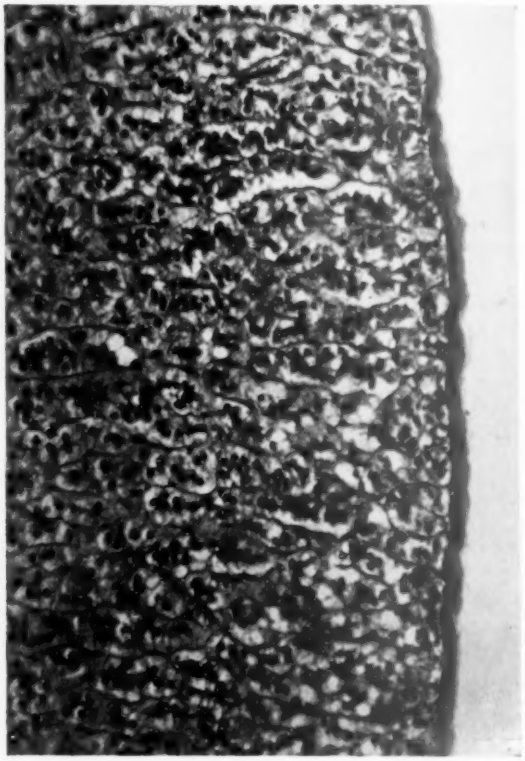

Fig. 12. Adrenal cortex (×280). Animal Group IV killed six weeks after irradiation.

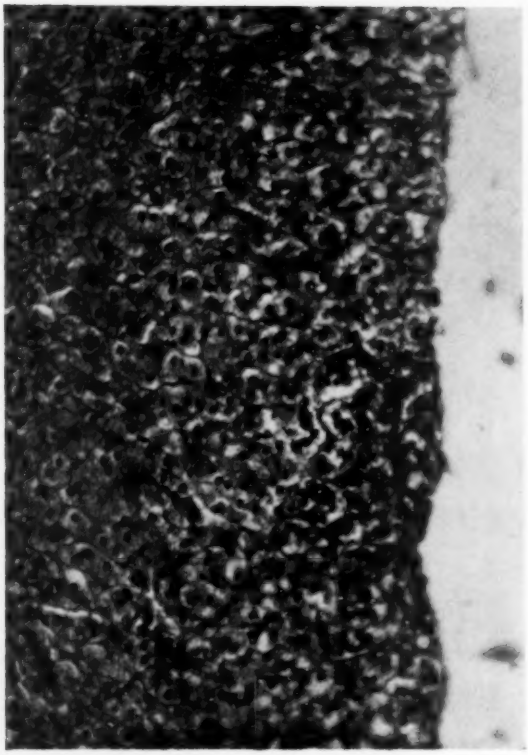

Fig. 11. Adrenal cortex (×280). Animal Group IV killed three weeks after irradiation.

tion and corpus luteum formation occur naturally only after copulation. It seems unreasonable to expect irradiation to initiate a cyclic process which does not occur normally.

Thyroid. The thyroid glands showed no demonstrable change in size. The histologic structure of the glands throughout the series was within the limits of normal variation as to the size of the acini, amount of colloid contained therein and the height of the epithelium (Figs. 7, 8 and 9).

Adrenals. The adrenals were normal in size and structure throughout the series. There was no evidence of degenerative changes in either the cortex or the medulla (Figs. 10, 11 and 12).

SUMMARY

In an effort to determine whether irradiation of the pituitary gland is harmful, adult female rabbits were irradiated in the region of the pituitary gland. The dosage was varied and when compared with that used in human therapy may be considered excessive. There was no disturbance in the normal physiological functions of these animals. The histological structure of the pituitary, ovaries, thyroid and adrenals showed no evidence of degenerative changes. The absence of anatomical changes cannot be interpreted as indicating lack of functional change. This could be determined only by studying a group of such animals over a period of time, breeding them and observing their offspring through several generations.

REFERENCES

1. Kotz, J., and Parker, Elizabeth. Treatment of female endocrinopathies. *Radiology*, 1938, *31*, 66–72.
2. Lawrence, J. H., Nelson, W. O., and Wilson, H. Roentgen irradiation of the hypophysis. *Radiology*, 1937, *29*, 446–454.
3. Hartman, C. G., and Smith, C. Non-effect of irradiation of hypophysis in sterile monkey females. *Proc. Soc. Exper. Biol. & Med.*, 1938, *39*, 330–332.
4. Shay, H. Quoted by A. T. Rasmussen in personal communication.
5. Dawson, A. B., and Friedgood, H. B. Differentiation of two classes of acidophiles in anterior pituitary of female rabbit and cat. *Stain Technol.*, 1938, *13*, 17–21.

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EDITORIALS

THE NECESSITY FOR RADIATION PROTECTION

"SAFETY" and "protection" are two overworked words at the present time, but they are two words which the radiologist might well add to his vocabulary and ponder their exact meaning in carrying out his daily routine of roentgen examinations and the use of the roentgen ray and radium in therapy. In spite of the fact that at the International Congress of Radiology held in 1928, 1931, 1934, and 1937 there were adopted proposals covering the broader aspects of roentgen-ray and radium protection, these proposals have received too little attention even by those who head many of the departments of radiology in the hospitals scattered across the country.

In January, 1941, was published an article by L. S. Taylor,[1] authorized by the Council on Physical Therapy of the American Medical Association, calling attention to the factors which offer protection from the roentgen ray. This thorough report quite comprehensively detailed the essentials of protection necessary in shielding the operator from direct radiation, scattered radiation and the protection that is essential in roentgenoscopy and roentgenography and the necessary materials to bring about adequate protection, and also considered the tolerance dose, in addition to some elementary safeguards from electrical shocks. His report was in summation the various proposals which have been recommended throughout the years from 1928 on.

Many reports have appeared in the literature calling attention to the presence of radiodermatitis among physicists, and as recently as May, 1941, Leddy and Rigos[2] noted the evident increase of roentgen-ray dermatitis among physicians which condition can only be minimized by the use of proper equipment and precise technique, protection devices and by experience and knowledge of those engaged in using roentgen rays, radium or radon, no matter how infrequently. They pointed out that of the measures for increasing safety, education is the most valuable and they called particular attention to the careless ones who think that roentgenologic technique is easily acquired and is safe. There are enormous risks in the casual use of the roentgenoscope by those without special training; mechanical equipment, quite rightly they say, cannot be substituted for mental equipment in roentgenology or any other branch of medicine.

The importance of this subject is again emphasized by Scheele and Cowie[3] as a result of their analysis of radiation protection in forty-five hospitals which they visited. These hospitals were of all types ranging in size from forty-four to over three hundred beds; thirty-two of the hospitals had more than two hundred beds. These investigators studied the storage and handling of radium, the calibration and shielding of roentgen therapy equipment and techniques of use and shielding of roentgenographic and roentgenoscopic units, and they used a standard of adequacy of equipment and practices based in most instances on the recommendations for protection which have been published by various writers and the standards of protection which have been recommended by the various radiological societies and particularly those recommended by the National Bureau of Standards.

[1] Taylor, L. S. X-ray protection. *J. Am. M. Ass.*, Jan. 11, 1941, *116*, 136–140.

[2] Leddy, E. T., and Rigos, F. J. Radiodermatitis among physicians. AM. J. ROENTGENOL. & RAD. THERAPY, May, 1941, *45*, 696–700.

[3] Scheele, L. A., and Cowie, D. B. Radiation protection in forty-five hospitals. *J. Am. M. Ass.*, Aug. 23, 1941, *117*, 588–591.

Their investigation is a rather severe indictment of the careless use of the roentgen ray and radium as regards the operator and technicians, and from an analysis of their study in these forty-five hospitals they conclude that there are many points in mechanics and practices which must be carefully controlled if overexposure to the operator and technician is to be avoided. In general they found that the hospitals tended to have good protection in most particulars or inadequate protection in most particulars. In those hospitals where careful compliance with the recommendations for protection against radium and roentgen rays were practiced even the busiest workers received only a daily dose in the order of 0.02 roentgen or less, but in many instances much more than the recommended exposure of 0.1 roentgen a day was received. The heads of the departments of radiology in the hospitals visited, they found, paid too little attention to adequate education and supervision of technical workers handling roentgen-ray and radium equipment. Obsolete equipment and failure to provide or use lead protective barriers during roentgenography permitted many cases of overexposure to occur. Considerable excessive exposure was found to result from the commonly observed practice of holding patients during roentgenography. It is, however, during the roentgenoscopic observations that both radiologist and technicians receive considerably more exposure than they are aware of and in the entire survey the most excessive exposure was noted during roentgenoscopy.

Scheele and Cowie call attention to the well known observation that considerably less inherent protection has been built into most equipment and protective devices than radiologists generally realize. Too often the manufacturers turn out a beautiful piece of equipment so far as the mechanism and appearance of the apparatus goes, giving too little thought to the protective measures which should be built into the apparatus. They gained the impression that too little attention has been paid to protection with reference to both equipment and practices in most of the hospitals visited, and that not enough attention has been given to the study of tolerance doses, the problems of shielding equipment and operating techniques.

It is imperative that all those who work in the roentgen-ray departments and handle radium must pay more strict attention to the protection devices already available and it is earnestly urged that all departments make use of the services of the qualified physicists[4] in determining whether or not there is sufficient protection in the apparatus used and in the rooms in which the radiologists carry on their daily routine. These physicists, as a result of their studies, can very soon point out the defects in the protective measures which are in existence in the various departments and, as has so aptly been pointed out by Quimby,[5] the physicist is very often able to pick up difficulties and shortcomings in the equipment and installation before it is even suspected by the radiologist. Elsewhere in this Journal there is a report by Taft[6] of stray radiation under actual conditions.

Too little attention is being paid to these all-important problems which really amount to self preservation. Not only should more attention be given to the protective measures that are inherent in the equipment and in the place of work, but other measures of protection such as frequent vacations for those who spend their time in the roentgen-ray and radium departments are imperative if the workers are not to suffer as a result of the use of so potent an aid in diagnostic and therapeutic medicine.

[4] Am. J. Roentgenol. & Rad. Therapy, June, 1941, *45*, 933.
[5] Quimby, E. H. Discussion of paper by Scheele and Cowie.
[6] Taft, R. B. Stray radiation under actual conditions. Am. J. Roentgenol. & Rad. Therapy, Sept., 1941, *46*, 373–375.

G. W. C. KAYE
1880–1941

THERE can be few if any men who are not in the medical profession to whom all roentgenologists owe so much as to G. W. C. Kaye. As a student at the Royal College of Science, London, physics was his chosen subject, and later, working as an advanced student at the Cavendish Laboratory at Cambridge, he came under the influence of J. J. Thompson and acted as his personal assistant. Here he was surrounded by a number of research workers whose names will go down in history in the annals of science—C. T. R. Wilson and F. W. Aston, to mention only two. Rutherford had just left to take the chair of physics at McGill, after completing his early pioneer

work in this laboratory. The study of the new radiations, on which so many of the researchers in this laboratory were engaged, was a virgin field of scientific investigation, one that was full of bewildering possibilities as the workers explored further and further into uncharted worlds. In this early work Kaye played his part, to some extent anticipating and laying the foundations of the later work by Moseley on the characteristic series of X radiations emitted by all elements. Incidentally, he took a keen interest in the Territorial Army, and when war broke out in 1914 he served with the Royal Engineers, but later was transferred to the Royal Flying Corps, in which he was promoted to the rank of Major, his post being that of chief inspector of materials for the Air Ministry. He also served on the Committee set up to advise the War Office on the use of roentgen rays in the Army. It was this work which brought him into close touch with the application of radiations to medicine, a contact that he studiously cultivated when, in 1922, he was appointed Superintendent of the Physics Department of the National Physical Laboratory, a post which he held until his death. In this Department, with its vast resources, he constantly strove to arrive at scientific bases for the application of radiations in medicine. A section for the measurement of the content of radium applicators was set up and Kaye worked for long to arrive at a satisfactory standard of measurement of radiations.

The tragedies of the pioneers who suffered from the effects of roentgen rays made a deep impression on Kaye, and he willingly consented to serve on a committee (The Radium and X-Ray Protection Committee) set up shortly after the war to tackle the formidable task of attempting to draw up recommendations as to the manufacture and use of radium and roentgen-ray apparatus that would make it impossible for a reasonably careful worker to sustain damage. An immense amount of labor went into the recommendations that were finally issued and a large proportion of the work, both on the experimental side and in the drafting of the reports, was done by Kaye. What a vast amount of work and argument would have been saved had the unit, the roentgen, been available at that time! Somewhat grudgingly these British recommendations were generally accepted in the country and were of great value, not only in bringing pressure to bear on hospitals to replace old and unsafe apparatus, but also in attaining satisfactory working conditions in departments, for in the early days any dark, disused cellar was considered good enough for roentgenologic work. Ventilation was the last thing to be thought of.

The facilities of the National Physical Laboratory for the inspection of apparatus and of departments were placed at the disposal of all who asked, and manufacturers could have their apparatus tested and certified by the National Physical Laboratory as complying with the standards recommended by the Protection Committee. Many unsatisfactory roentgenologic departments were condemned and rebuilt as the result of Kaye's report on behalf of the National Physical Laboratory.

At the First International Congress of Radiology, held in London in 1925, a committee was appointed with Kaye as chairman to draw up recommendations for the protection of workers. It speaks volumes for the soundness of the spade work which was so largely Kaye's that the recommendations of the British Radium and X-Ray Protection Committee were accepted with no alteration of any consequence. The unanimous acceptance of the international unit of radiations was very largely due to Kaye's clear-sighted presentation and advocacy of it before the International Congresses of Radiology in London (1925) and Stockholm (1928). The actual proposal that the unit should be related to the ionization in air was, however, the suggestion of Sir William Bragg. This contribution brought order out of chaos and made possible the great advances that have followed in its wake—radiotherapy became a science largely as the result of this fundamental advance.

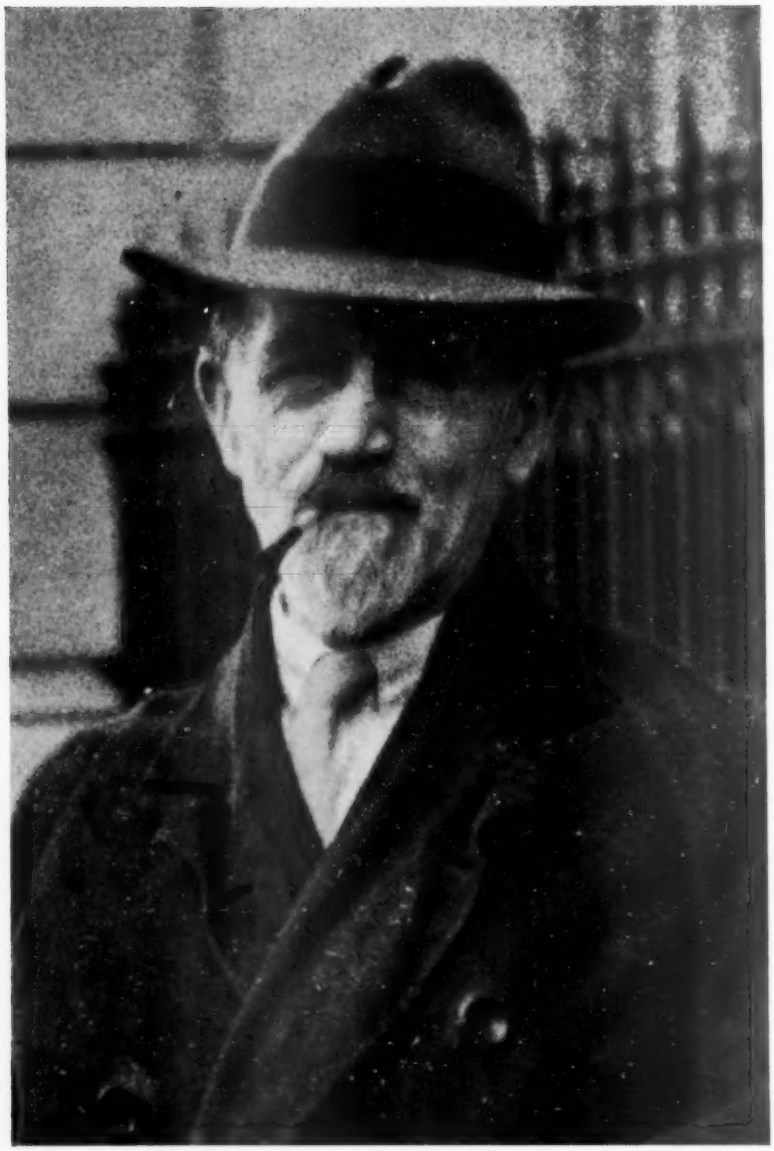
Another of Kaye's many activities was the study of architectural acoustics. He and his collaborators also designed apparatus for the measurement of the intensity of various types of noise. His small book "X-Rays" has gone through many editions. Kaye and Laby's "Tables" of physical constants is used by all physicists and chemists. In acknowledgment of his many contributions to science Kaye was elected as a Fellow of the Royal Society—a richly deserved honor.

Kaye published many important papers, often in collaboration with fellow workers, on the physics of radiations, the majority being more or less directly concerned with the applications of the rays to medicine. One often felt that he regretted he had not studied medicine. This perhaps explains why he held so tenaciously to his medical contacts in spite of the pressure of other work—to the very great advantage of roentgenologists. He was particularly interested in cancer, and not only served on the committee of the Cancer Hospital but was also an active member of the Grand Council of the British Empire Cancer Campaign.

Kaye joined the Röntgen Society (founded in 1897) in 1913 and became its President in 1917. When this Society was incorporated with the British Institute of Radiology, which was purely medical, Kaye's influence was decisive, and he played a leading part in preserving the scientific side while welding the diverse interests that were brought together by this amalgamation. He became President in 1928 and was joint editor of its journal, the *British Journal of Radiology*, for thirteen years. He delivered most of the prized English memorial lectures connected with roentgenology, but the invitation that gave him greatest pleasure was that from the American Roentgen Ray Society to contribute the Caldwell Memorial Lecture in 1927. The title of this lecture was "Some fundamental aspects of roentgen rays and the protection of the roentgen-ray worker." In the proceedings and organization of the International Congresses of Radiology he took a very active part. He was always one of the physicist members of the British delegation and, as already mentioned, was himself very largely responsible for the adoption of the international recommendations for protection and for the international standard of radiations.

Kaye was a quiet, reserved man, who inspired confidence and was not easily perturbed. He was an ideal committee man; wise, constructive, informed, and gently persistent, he carried great weight. Moreover he never spared himself in working for the many committees on which he served. If he saw something that needed doing he did it, often at great personal inconvenience and sacrifice of time. His enthusiasm for the development of the application of radiations to medicine made this kindly, sensitive and lovable man one of those with whom differences of opinion and outlook did not break friendship. With the passing of G. W. C. Kaye, roentgenologists throughout the world have lost a true and loyal friend.

A. E. Barclay



WILLIAM CLARK WESCOTT
1868–1941

DR. WILLIAM CLARK WESTCOTT died on July 26, 1941, at the age of seventy-three, of coronary occlusion following a short illness.

When he graduated from the University of Pennsylvania with the degree of M. D. in 1908 at the age of forty, Dr. Westcott was already well known as a roentgenologist. As the proprietor of a drug store in Atlantic City, which position he had attained by working after hours since the age of thirteen, he installed a static machine which he used successfully for roentgenography; and as a medical undergraduate he spent as much time as possible in the roentgen-ray department of the Atlantic City

Hospital. His study of medicine was in recognition of the necessity of medical knowledge in the interpretation of roentgen findings. Thus he virtually grew up in the hospital which he served for many years as chief of the department of radiology.

An insatiable traveler, Dr. Westcott made many trips to Europe and was well acquainted with the outstanding specialists of the Old World. He was a corresponding member of the Vienna Roentgen Society; in addition he was a member of the American Roentgen Society and the Radiological Society of North America, of which he served a term as vice-president; a fellow of the American College of Radiology, and a member of Sigma Xi. Though a non-resident member, he was active in the affairs of the New York Roentgen Society, a group which will miss him very sadly.

Ramsay Spillman

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. C. B. Peirce, Royal Victoria Hospital, Montreal, Canada. Annual Meeting: 1942, to be announced.

American College of Radiology
Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill. Annual meeting: Atlantic City, N. J., June 10, 1942.

Section on Radiology, American Medical Association
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: Atlantic City, N. J., June 8–12, 1942.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: Fairmont Hotel, San Francisco, Calif., Nov. 30–Dec. 5, 1941.

Radiological Section, Baltimore Medical Society
Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

Section on Radiology, California Medical Association
Secretary, Dr. J. D. Coate, 434 Thirtieth St., Oakland, Calif.

Radiological Section, Connecticut Medical Society
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets bi-monthly on second Thursday, at place selected by Secretary. Annual meeting in May.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill.

Radiological Section, Los Angeles Co. Med. Soc.
Secretary, Dr. Wilbur Bailey, 2007 Wilshire Blvd., Los Angeles, Calif. Meets on second Wednesday of each month at County Society Building.

Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas.

Brooklyn Roentgen Ray Society
Secretary, Dr. Leo Harrington, 880 Ocean Ave., Brooklyn, N. Y. Meets monthly on fourth Tuesday, October to April.

Buffalo Radiological Society
Secretary, Dr. Joseph S. Gian-Francheschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months.

Chicago Roentgen Society
Secretary, Dr. C. J. Challenger, 3117 Logan Blvd. Meets second Thursday of each month October to April inclusive at the Palmer House.

Cincinnati Radiological Society
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

Cleveland Radiological Society
Secretary, J. O. Newton, 13921 Terrace Rd., East Cleveland. Meets at 6:30 P.M. at Midday Club on fourth Monday each month, October to April, inclusive.

Denver Radiological Club
Secretary, Dr. P. R. Weeks, 520 Republic Bldg., Denver, Colo. Meets third Friday of each month.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

Florida State Radiological Society
Secretary, Dr. J. N. Moore, 210 Professional Bldg., Ocala, Florida. Meetings in May and November.

Georgia Radiological Society
Secretary, Dr. R. C. Pendergrass, Prather Clinic Bldg., Americus, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

Illinois Radiological Society
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. H. C. Ochsner, Methodist Hospital, Indianapolis. Meeting held the second Sunday in May annually.

Kentucky Radiological Society
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in April.

Long Island Radiological Society
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

Louisiana Radiological Society
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society meeting. Next meeting New Orleans, April, 1942.

Michigan Association of Roentgenologists
Secretary, Dr. J. E. Lofstrom, 1536 David Whitney Bldg., Detroit. Three meetings a year, Fall, Winter, Spring.

Milwaukee Roentgen Ray Society
Secretary, Dr. I. I. Cowan, Mt. Sinai Hospital, Milwaukee, Wis. Meets monthly on first Friday at University Club.

Minnesota Radiological Society
Secretary, Dr. J. P. Medelman, 572 Lowry Medical Arts Bldg., St. Paul.

Nebraska Radiological Society
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. A. O. Hampton, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

Radiological Society of New Jersey
Secretary, Dr. H. J. Perlberg, 921 Bergen Ave., Jersey City. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

New York Roentgen Society
Secretary, Dr. E. J. Ryan, St. Luke's Hospital, New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

North Carolina Roentgen Ray Society
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

Central New York Roentgen Ray Society
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year. January, May, November.

Ohio Radiological Society
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati. Meets at time and place of annual meeting of Ohio State Medical Association.

Pacific Roentgen Society
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

Philadelphia Roentgen Ray Society
Secretary, Dr. B. R. Young, Temple University Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

Pittsburgh Roentgen Society
Secretary, Dr. H. W. Jacox, 4800 Friendship Ave. Meets second Wednesday each month, 4:30 P.M., October to June, Pittsburgh Academy of Medicine.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. S. C. Davidson, 277 Alexander St. Meets on second Thursday from October to May, inclusive. 8 P.M., Rochester Academy of Medicine Building.

Rocky Mountain Radiological Society
Secretary, Dr. A. M. Popma, 220 N. First St., Boise, Idaho. Annual meeting in Denver, summer of 1942.

St. Louis Society of Radiologists
Secretary, Dr. W. K. Mueller, University Club Bldg. Meets fourth Wednesday of October, January, March and May, at a place designated by the president.

San Francisco Radiological Society
Secretary, Dr. H. A. Hill, 450 Sutter St., San Francisco. Meets monthly on third Thursday at 7:45 P.M., first six months at Toland Hall, second at Lane Hall.

South Carolina X-Ray Society
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

Tennessee Radiological Society
Secretary, Dr. F. B. Bogart, 311 Medical Arts Bldg., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. L. W. Baird, Scott and White Hospital, Temple, Texas.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Radiological Society
Secretary, Dr. C. H. Peterson, 603 Medical Arts Bldg., Roanoke, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. K. J. Holtz, American Bank Bldg., Seattle. Meets fourth Monday each month, College Club, Seattle.

X-Ray Study Club of San Francisco
Secretary, Dr. J. M. Robinson, University of California Hospital. Meets monthly in evening on third Thurday.

Cuba

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets monthly on third Thursday from November to June inclusive, at 8:15 P.M., 32 Welbeck St., London.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine, 1, Wimpole St., London, W. 1.

Faculty of Radiologists
Secretary, Dr. M. H. Jupe, 32 Welbeck St., London, W. 1, England.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to November inclusive.

Canadian Association of Radiologists
Secretary, Dr. A. C. Singleton, Medical Arts Bldg. Toronto, 5, Ontario.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext., Halifax, N.S.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

Continental Europe

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel. Meets annually in different cities.

Societa Italiana Radiologia Medica
Secretary, Prof. M. Ponzio, University of Turin, Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 P.M.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Orient

Japan X-Ray Association
c/o Orthopedic Surgery, Tokyo Imperial University. Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto, Japan. Meets bi-monthly on third Sunday.

BULLETIN OF THE INTER-SOCIETY COMMITTEE FOR RADIOLOGY

THE EMPLOYMENT OF PHYSICIANS BY HOSPITALS: SOME LEGAL ASPECTS

By MAC F. CAHAL

(*Continued*)

Eleemosynary Institutions

In what is apparently a conscious intent to cloud the issue, some writers have pointed to the fact that if the employment of a physician creates the master-servant relationship between the physician and his employer, medical schools have long been engaged in the practice of medicine and have occupied the position of a principal by employing physicians. The answer is, of course, that so long as the charging and collecting of a fee is lacking and so long as the institution is not selling the services of its servants for its own profit, the customary principles of agency do not apply, as evidenced by the adjudicated cases.[51] In the case of charity patients, liability on the part of the hospital can be avoided by resort to the implied waiver of liability by a beneficiary, or to the "trust fund" theory that the dissipation of public funds is contrary to public policy. In the case of private paying patients, on the other hand, it would seem that the general rules applying to private hospitals should apply.[52]

The fact that benevolent corporations have been held not liable for the torts of employed physicians does not prove that such hospitals are not engaged in the practice of medicine. It simply proves they are not liable under the doctrine of *respondeat superior*. To these institutions the comment of the Restatement may be applied: "The normal status of a physician employed by one person to render medical services to another is that of an independent contractor, responsible to the master, not for the manner but only the results of his service."[53] But, obviously, he could not be an independent contractor in those cases holding the hospital liable for his negligence. When a charity patient is admitted for treatment to an eleemosynary institution, the physician's relation to the corporation employing him is analogous with his relation to the parent or guardian of a child, who engages his services for the child. It is simply the case of one person (for convenience the law resorts to a fiction and regards the corporation in certain matters as a person) obtaining and paying for medical services rendered by a physician to a dependent third party.

Under this theory, benevolent associations not operated for profit have been held not to be engaged in the practice of medicine by furnishing the services of physicians to members.[54] It is significant, however, that in most of these tort cases the question of agency has been circumvented by finding an implied waiver of liability by the beneficiary, or resorting to the trust fund theory.[55] Too, the "loaned servant" doctrine has been invoked to exempt charitable hospitals from liability for torts of its employees while assisting an attending physician or surgeon.[56]

Another line of cases to be distinguished from those holding a hospital corporation liable for the torts of its employees are those in which an employer or any third person has been held as not liable in an action of law for malpractice perpetrated by a physician whose fees are paid by the employer. Most railway physicians and industrial surgeons are to be found under this category. Here no profit ensues to the employer or to

[51] In Rivers et al. v Atlanta Southern Dental College, 1 S.E. (2nd) 750, the college was enjoined against violating the dental practice act by treating patients in the college clinic and charging a fee therefor. In a number of states the charging of a fee is an essential element in bringing an act within the prohibitions of the medical practice act.

[52] England v Hospital of the Good Samaritan (Cal.) 88 Pac. (2nd) 727, 97 Pac. (2nd) 813; Sisters of the Sorrowful Mother v Zeidler (Okla.) 82 Pac. (2nd) 996.

[53] *Restatement, op. cit.*, Sec. 223. See Yale L. J. 348, and cases cited there.

[54] 119 A. L. R. 1284.

[55] England v Hosp. of the Good Samaritan, 16 Cal. App. (2nd) 640, 61 Pac. (2nd) 48 (1936); Hawthorne v Blythewood, 118 Conn. 617, 174 Atl. 81 (1934); D'Amato v Orange Memorial Hosp., 101 N. J. 127 Atl. 340; Mikota v Sister of Mercy Hosp., 183 Iowa 1378, 168 N. W. 219 (1918); Rudy v Lakeside Hosp., 155 Ohio St. 539, 155 N. E. 126 (1926); Bise v St. Luke's Hosp., 181 Wash. 269, 43 Pac. (2nd) 4 (1935).

[56] Armstrong v Wallace (Cal.) 37 Pac. (2nd) 467.

the third person. He does not charge the patient a fee; he merely agrees to pay for the services. Here the physician is an independent contractor, and not an agent or servant of the party paying for the services.[57]

Respondeat Superior

From an examination of the cases pertaining to the liability of an incorporated hospital for the torts of its employed physicians, we are forced to the conclusion that where a corporation employs a physician at a fixed stipend and reaps a profit from the fees charged for his services, the corporation itself charging and collecting fees for the physician's services, an agency relationship is created and the familiar doctrine of *respondeat superior* applies.

Occupying the position of principal in an agency relationship, the hospital is subject to another maxim in the law: *Qui facit per alium, facit per se.* The hospital is engaged in the practice of medicine.

Where a hospital merely undertakes to supply rooms, board, hospital facilities, nursing services and internes to act under the direction of the physician selected by the patient (loaned servant doctrine), the hospital is not practicing medicine. Where the corporation merely procures a member of the staff to attend the patient and the physician is not in the employment of the corporation, the corporation is not practicing medicine; the physician is an independent contractor answerable to the patient alone. Likewise, where the physician is an employee of the corporation, but his services are gratuitous, the doctrine of *respondeat superior* is usually not applicable.[58] These are special circumstances resulting in a departure from the prevailing rule.

Corporate Practice

Having applied the accepted maxims of agency, we have reached an affirmative answer to the first of the two questions presented in our opening: A hospital which employs physician on a salary or other stipulated compensation, the hospital charging and collecting fees for the physician's services, is, according to the general authority, itself engaged in the practice of medicine. We turn now to the second question presented: Is such practice lawful?

In an almost unbroken line of cases, the courts have answered this question in the negative. The common law rule forbidding the practice of law by corporations was long ago extended to apply to medicine and allied professional fields.[59]

In the absence of express statutory authority, the weight of judicial reason and authority favors the view that neither a corporation nor any other unlicensed person or entity may engage in the unlicensed practice of medicine through licensed employees. The reason for the rule may be stated in general to be the inability of a corporation to possess the specified requirements; its incapacity to qualify by taking a personal examination; and the recognition that because of the inherent characteristics of a corporation there can never exist between it and the patient that confidential and intimate personal relationship ordinarily present between physician and patient.[60] A corporation cannot be licensed to practice medicine because it cannot satisfy the requirements of the pertinent medical practice act.[61] Obviously, it cannot present evidence of educational or

[57] Borgeas v Oregon Short Line Ry. (Mont.) 236 Pac. 1069. ("The act of the servant becomes the act of the master, who has the right to control the manner in which he discharges his duties, and, when injury results, they are joint tortfeasors. But the relation of master and servant, or of principal and agent, does not exist between the railroad company as employer, and a surgeon employed to treat an injured employee, the reason being that the employer has no right to control the surgeon in the treatment of the case . . . ; and the rule of *respondeat superior* does not apply in the case of such employment.")

[58] Coldwater v Citizens Gas Co. (N. Y. Mun. Ct. 1938) 7 N. Y. S. (2nd).

[59] See 73 A. L. R. 1327 (1931) and cases cited there. (Optometry) 102 A. L. R. 334. State *ex rei* Beck v Goldman Jewelry Co., 142 Kans. 881; Funk Jewelry v State (1935) (Ariz.) 50 Pac. (2nd) 945; Eisensmith v Buhl Co. (1934) (W. Va.) 178 S. E. 695; Stern v Flynn (1935) 154 Misc. 609, 278 N. Y. S. 598. (Medicine) See 103 A. L. R. 1240, and cases cited there. ("The majority, though not all, of the decisions on the subject, hold that neither a corporation nor any other unlicensed person or entity may engage in the practice of medicine, surgery, or dentistry through licensed employees.") 19 C. J. Sec. 402. See 119 A. L. R. 1290. Cf. Silver v Lansburgh & Bros. *et al.* (D. C.) 27 F. Supp. 682, 111 F. (2nd) 518.

[60] McMurdo v Getter (Mass.) 10 N. E. (2nd) 139.

[61] From a memorandum prepared by the Bureau of Legal Medicine and Legislation of the American Medical Association.

moral qualifications nor can it pass the required examinations given by the licensing board.[62]

Since a corporation cannot legally practice medicine directly, it cannot do so indirectly by means of agents duly licensed to practice.[63]

After citing a few cases holding to the contrary,[64] the Bureau of Legal Medicine and Legislation of the American Medical Association states:

"The influence of these cases, however, has been negative on courts subsequently passing on the right of a corporation to practice medicine. The Lewin case seems never to have been cited or referred to by a court of appellate jurisdiction. The Liggett case, in which the United States Supreme Court held unconstitutional a Pennsylvania statute requiring drug stores to be owned by licensed pharmacists only, has been ably and logically distinguished from the problem presently involved by the Supreme Court of Colorado in *People v Painless Parker Dentist, 275 Pac. 928*, and by the Supreme Court of Illinois in *People v United Medical Service, Inc., 200 N. E. 157*.

"The Brown case in which the Supreme Court of Washington held unconstitutional a state statute forbidding any person other than a licensed dentist to own or operate a dental office, has been ignored in most of the more recent cases, has been expressly limited even in Washington (see *In re O'Neill, 41 Wash. 174*), and has been expressly repudiated by the Supreme Court of California in *Parker v Board of Dental Examiners, 14 Pac. (2nd) 67*. There the Supreme Court of California said:

'Appellant claims that there is a distinction between the practice of dentistry which the statute undertakes to regulate and the purely business side of the practice: that the first requires skill and learning, while the latter requires only training in business transactions, and if the management or conduct of the "business side" by a layman is inhibited by statute, then the inhibitions of the statute are beyond the scope of the police power of the state, and are void as being unconstitutional, citing *State v Brown, 37 Wash. 97, 79 Pac. 635*. . . . But we are not prepared to hold with the contention that a corporation or an unlicensed person may not be prevented from managing, conducting, or controlling what petitioner terms the "business side" of the practice of dentistry. The law does not assume to divide the practice of dentistry into that kind of departments. Either one may extend into the domain of the other in respects that would make such a division impractical if not impossible. The subject is treated as a whole . . .'

"The remaining cases that can be cited as authority for permitting a corporation to practice medicine are the two Nebraska cases involving State Electro-Medical Institute, *supra*. These cases have been expressly repudiated by the Supreme Courts of Colorado and Iowa, and no court of appellate jurisdiction has adopted their holding. The fallacious reasoning which the Nebraska court employed in arriving at the result it did is apparent. The court, while admitting that a corporation cannot be licensed to practice medicine, asserted that it was impossible for a corporation to practice, saying:

'It is impossible to conceive of an impersonal entity "judging the nature, character and symptoms of the disease," or giving or prescribing the application of the remedy to the disease. Members of the corporation, or persons in its employ, might do these things, but the corporation itself is incapable to do them. The qualification of a medical practitioner is personal to himself. The intention of the law is that one who undertakes to judge the nature of a disease . . . must have certain personal qualifications: and, if he does these things without having complied with the law, he is subject to its penalties. Making contracts is not practicing medicine. Collecting the compensation therefor is not practicing medicine within the meaning of this statute. No professional qualifications are requisite for doing these things.' "

The author wishes here to express his appreciation for the generous and valuable assistance rendered by Mr. T. V. MacDavitt and Mr. J. W. Holloway, Jr., acting director of that Bureau.

[62] People v Painless Parker Dentist (Colo.) 275 P. 928. State v Bailey Dental Co. (Iowa) 234 N. W. 260; People v United States Medical Service, Inc. (Ill.) 200 N. E. 157; Com. *ex rel.* Attorney General v Alba Dentists Company, 13 Pa. D. R. 432.

[63] People v John H. Woodbury Dermatological Institute (N. Y.) 85 N. E. 697; Hannon v Siegel-Cooper Co. (N. Y.) 60 N. E. 597; People *ex rel.* Lederman v Warden of City Prison 152 N. Y. S. 977; Granger v Adson *et al.* (Minn.) 250 N. W. 722; Winslow v Kansas State Board of Dental Examiners, 14 Pac. (2nd) 67; People *ex rel.* State Board of Medical Examiners v Pacific Health Corporation, Inc. (Cal.) 82 Pac. (2nd) 429; Benjamin Franklin Life Assur. Co. v Mitchell Insurance Com'r. (Cal.) 58 Pac. (2nd) 984; Pacific Employers Ins. Co. v Carpenter (Cal.) 52 Pac. (2nd) 992. ("It is clearly declared unlawful for a corporation to indirectly practice any of said professions for profit by engaging professional men to perform professional services for those with whom the corporation contracts to furnish such services. In other words, said authorities declare that said professions are not open to commercial exploitation and it is said to be against public policy to permit a 'middleman' to intervene for profit in establishing the professional relationship between the members of said profession and the members of the public.") State Board of Dental Examiners v Walsh (Colo.) 8 Pac. (2nd) 704. State v Williams (Ind.) 5 N. E. (2nd) 961.

[64] Memorandum *supra*. State *ex inf.* Sager v Lewin (Mo.) 106 S. W. 581; Louis K. Liggett Co. v Baldridge, Atty. General of Pa., 49 Sup. Ct. 57; State v Brown (Wash.) 79 Pac. 635; State-Electro Medical Institute v State (Neb.) 103 N. W. 1078; State-Electro Medical Institute v Platner (Neb.) 103 N. W. 1079.

It is manifest that the Supreme Court of Nebraska, in reaching this conclusion, lost sight of the fact that a corporation is an intangible creature of the law that can act only through human agents and that the acts of the agents are attributed to the corporation. For instance, a public service corporation does not by its intangible self directly maintain its power plant, distribute electricity, and operate its conveyances. The intangible corporation itself cannot perform these physical acts. It hires men to do them. Yet no one for a moment says that the "corporation" cannot and does not provide electricity and transportation. By no reasonable process of logic, then, can one say that when a corporation employs licensed physicians to diagnose cases of illness and to treat them, the corporation itself is not practicing medicine.

The principles stated above are as applicable to a corporation composed solely of licensed physicians as they are to any other corporation. A corporation is an entity separate and apart from its members. Its authority and power is derived solely from its charter and from pertinent state statutes. It derives no authority and no power by virtue of the qualifications of its component members. The fact that every member of a corporation is licensed to practice medicine does not endow that corporation with any authority to practice medicine. In this connection, with respect to the practice of law by a corporation composed solely of members of the Bar, an appellate court of California said in *People ex rel. Los Angeles Bar Assn. v California Protective Corporation (1926), 76 Cal. App. 354,* 244 Pac. 1089:

> It is true that individuals who are duly licensed members of the bar may "lawfully" associate themselves in any unincorporated form of association, such as a partnership, for the practice of law. But such individuals may not associate themselves for the practice of law under the aegis of a corporation. Though all the directors and officers of the corporation be duly licensed members of the legal profession, the practice of law by the corporation would be illegal, nevertheless. At any time those directors and officers, by death or by transfer of their shares, might be succeeded by laymen none of whom possessed the right to practice law.

An auto club was held to be practicing law though a practically unlimited choice of attorneys was given the members.[65] Despite the fact that the Illinois statute prohibiting the corporate practice of law expressly provides that it does not apply to corporations not-for-profit, the rule has been applied to corporations organized not-for-profit and which were engaged in the practice of law.[66]

Notwithstanding the argument that the ethical considerations required by the medical profession are satisfied when the profit motive is eliminated as in the case of eleemosynary institutions, the personal relationship essential to good medical practice is impaired. One of the best comments on this subject is that contained in *McMurdo v Getter (Mass.) 10 N. E. (2nd) 139,* which involved the unlawful practice of optometry. In that case, after discussing the licensing of certain businesses, the court said in part:

> . . . A different rule has been applied to the learned professions. These are characterized by the need of unusual learning, the existence of confidential relations, the adherence to a standard of ethics higher than that of the marketplace and in a profession like that of medicine by intimate and delicate personal ministration. Traditionally, the learned professions were theology, law and medicine; but some other occupations have climbed and still others may climb to the professional plane. . . . Dentistry, a branch of medicine, has done so within modern times. Professional men may be held to a higher ethical code, for example, by the restriction of advertising, than one engaged in ordinary business. . . . The rule is generally recognized that a licensed practitioner of a profession may not lawfully practice his profession among the public as the servant of an unlicensed person or corporation; and that, if he does so, the unlicensed person or corporation employing him is guilty of practicing that profession without a license. A corporation as such cannot possess the personal qualities required

[65] *In re* Maclub of America (Mass.) (1936) 3 N. E. (2nd) 272.

[66] People v Motorists' Assn. of Ill., 354 Ill. 595, 188 N. E. 827; People *ex rel.* Courtney v Assn. of Real Estate Taxpayers, 354 Ill. 102, 187 N. E. 823; People v Chicago Motor Club, 362 Ill. 50, 199 N. E. 1.

of a practitioner of a profession. Its servants, though professionally trained and duly licensed to practice, owe their primary allegiance and obedience to their employer, rather than to the clients or patients of their employer. The rule stated recognizes the necessity of immediate and unbroken relationship between a professional man and those who engage the services. . . . In the absence of statutory modifications in favor of hospitals or others . . . the same rule (as to lawyers) applies to physicians and dentists.

The "Group Health" Case

In the recent much-discussed case of the Group Health Association in Washington,[67] The District of Columbia Court held that a corporation organized not for profit to engage in the practice of medicine was not in violation of the law. Said the court, "Such a corporation, not for profit but for the mutual benefit of its members, is in my opinion not engaged in the practice of medicine, or in holding itself out as doing so. It is true that a corporation can act only through its agents and employees, but the physicians with whom the plaintiff makes contract are rather in the position of independent contractors, and the plaintiff does not in any way undertake to control the manner in which they attend or prescribe for patients."

We have seen that the great weight of authority is contra.[68] We have likewise seen that the fact of control is not determining—it is the right of control, a right which invariably exists in the relationship of employer and employee. The courts have repeatedly asserted that the practice of a profession cannot be divided into departments, on one side the performance of service and on the other the management of the financial relationship.[69] The law has wisely refused to allow a third party to shift the allegiance of the practitioner from the patient to himself.

In commenting on the Group Health case and the question there involved, Joseph Laufer, referring to the majority view, states that, "Although the corporation's inability to act physically is recognized, the acts of its agents are attributed to it. The corporation is then treated as a human actor. Where the act is the practice of medicine, the corporation itself is said to practice and, being unlicensed, is held guilty of violating the Licensure Act. The flaw in this reasoning lies in its anthropomorphism."[70]

Here is the profound principle involved. The truth is that the whole philosophy of medicine is founded upon a spirit of anthropomorphism. Its concepts are, first and last, humanistic. Every consideration, legal, economic, or scientific, must be examined in terms of its human values—of its application to the welfare of a single human being, the patient.

The science and the ethics of medicine did not spring from the market-place. They were born in the temple of Aesculapius and nurtured in the individual hands of many generations of physicians. The sufferings of a sick man can be relieved only by the ministrations of another man—the physician. That is why the corporation, so convenient for the machinations of modern-day business, is alien to the personal and intimate relationship which surrounds the care of the sick and dying.

The doctrine forbidding the practice of medicine by corporations has found expression in our system of jurisprudence under the sound reasoning that the interjection of a third party between a doctor and his patient destroys the close relationship so important in the treatment of sickness. As with other settled principles in the law, it is founded upon considerations for the benefit of mankind and the welfare of our society.

[67] Group Health Assn. v Moor (D. C.) (1938) 24 F. Supp. 445, 107 Fed. (2nd) 703. See "The American Medical Association and the Anti-Trust Laws," 8 Fordham L. R. 1, Jan. 1939, p. 82.

[68] *Supra.*, footnote 58.

[69] Parker v Board of Dental Examiners, 216 Cal. 285, 14 Pac. (2nd) 67; Dr. Allison, Dentist, Inc. v Allison, 360 Ill. 368, 196 N. E. 799. ("A corporation cannot qualify to practice a learned profession, since it can have neither honesty nor conscience and its loyalty must be rendered to its managers, directors, and stockholders.")

[70] Laufer, *Law and Contemporary Problems*, Duke University School of Law, 1939, 6, 525.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

HEAD

Lorenz, Reinhold. Zur Lagebestimmung der verkalkten Glandula pinealis im Röntgenbild. (The determination of the position of the calcified pineal gland on the roentgenogram.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, June, 1940, *61*, 338–348.

Schüller (1909) was the first to describe lateral displacement of the pineal gland as a sign of brain tumor. Estimates of the incidence of calcification of the pineal gland vary from 17 to 58 per cent. The author has studied the incidence in various age groups when the examination was made for an injury, thus ruling out the influence of disease. The earliest definite calcification was demonstrated in an infant twelve months of age. The incidence obtained for various age groups was as follows:

Age (yr.)	1–5	6–10	11–15	16–18	19
Incidence	6.9%	17.1%	34.8%	44.1%	57.9%
Age (yr.)	20	20–50	50–60	60	
Incidence	68.8%	72.1%	78%	78.8%	

The older methods of estimating the position of the pineal gland are summarized. One of the difficulties in measuring lateral displacement has been in obtaining a true sagittal projection. This is obviated if one bisects a line drawn between the tips of the mastoid processes and erects a perpendicular at the point of bisection. If the pineal gland is not displaced this line will pass through it whether or not the skull is rotated from a true sagittal position. A quicker method is to use a compass with the pineal gland as the center of a circle which should include the tips of both mastoid processes on the circumference.

The author's method for the lateral exposures is to measure the angle between a line drawn through the junction of the floor of the skull with the internal table of the frontal bone and the upper edge of the petrous ridge and a line drawn through the same point anteriorly and the pineal gland posteriorly. The incidence of the values obtained in cases is as follows:

Angle		12°	13°–17°	18°–19°	20°
Incidence	20 yr.	0%	81.9%	14.8%	3.3%
	20–50 yr.	1.4%	96.0%	2.6%	
	50– yr.	0%	98.8%	1.2%	

By far the most frequently encountered values were 15° and 16°.

A further observation has been that a circle with its center at the intersection of the lines mentioned above and drawn through the pineal gland will in normal instances pass through the porus acusticus. A 5 mm. variation may be allowed each way.—*W. A. Evans, Jr.*

Schüller, Arthur. The diagnosis of "basilar impression." *Radiology*, Feb., 1940, *34*, 214–216.

Basilar impression is a name given to various types of deformity of the posterior fossa of the skull and the upper cervical vertebrae. It may be caused by decalcification of the bones, long-standing increased intracranial pressure or congenital malformation in the atlanto-occipital region. Generally the weighted parts of the occiput which form the frame of the foramen magnum are pushed up toward the cranial cavity. Individuals with this deformity have a charac-

teristic short neck. Basilar impression may not cause any symptoms throughout life. In other cases there are symptoms caused by pressure on the spinal cord, the nerves in the posterior fossa and the cerebellum.

The picture due to this deformity is shown clearly in lateral and anteroposterior roentgenograms. Diagrammatic sketches of the position of the bones are given. Roentgen examination in such cases helps to prevent mistaken diagnoses and save the patient unnecessary operation. The condition is frequently mistaken for syringomyelia, syringobulbia, Klippel-Feil syndrome or tumor of the cerebellum.—*Audrey G. Morgan.*

Malone, L. A. Odontomas. *Radiology*, May, 1940, *34*, 573–576.

Every primary tumor of the jaw originating in one or more of the dental formative organs is an odontoma or tooth tumor. The most generally accepted classification of these tumors is that of the British Dental Association which is as follows: I. Epithelial odontomas: (A) Multilocular cysts; (B) Dentigerous cysts; (C) Dental cysts. II. Composite odontomas: (A) Irregularly calcified tumors: 1. Complex composite odontomas; 2. Compound composite odontomas; (B) Toothlike tumors: 1. Geminated composite odontomas; 2. Gestant composite odontomas; 3. Enamel nodules; (C) Dilated composite odontomas; 1. Dilated crown; 2. Dilated whole mass. 3. Dilated root. III. Connective-tissue odontomas: (A) Fibrous odontomas; (B) Cementomas. Brief descriptions of these different forms are given.

Treatment of all of them except multilocular cyst or adamantinoma is relatively simple, consisting of complete enucleation of the tumor and capsule with closure of the small cavities and packing of the large ones with iodoform gauze. In atypical root abscesses or cysts the tissue attached to the tooth should be sectioned to see whether there are any malignant changes. After removal of fibromas cauterization is indicated because of the possibility of sarcomatous degeneration.

A case of complex composite odontoma is described and illustrated with a roentgenogram. It was in a negro child seven years of age and was removed intra-orally bit by bit with particles varying in size from small granules to that of a large kidney bean.—*Audrey G. Morgan.*

Diamant, Marcus. Otitis and size of the air cell system. *Acta radiol.*, 1940, *21*, 543–548.

The question of the relation between otitis and the size of the air cell system in the mastoid bone has been discussed a great deal recently. The earlier opinion that chronic otitis results in sclerosis of the bone with disappearance of a previously existing cell system has been given up. It is now generally believed that small cell systems predispose to chronic otitis, while acute otitis is apt to develop in persons with large cell systems.

In order to study this question the author made roentgen examinations of the size of the cell systems in 320 normal individuals and in 585 cases of otitis of different types. The roentgenograms were made in the lateral projection and the measurements made with a planimeter and recorded in square centimeters. A table showing the details of the results is given.

The examinations showed that, as a general rule, individuals with chronic otitis with marginal perforation had very small cell systems, those with chronic otitis with central perforation somewhat larger cell systems, and in cases with scars in the tympanic membrane, indicating a healed chronic otitis, the cell system was still somewhat larger. The average size of the air cell system in cases of acute otitis was larger than in cases of chronic otitis, but smaller than in normal persons. Moreover the examinations showed, among other things, that persons with air cell systems larger than 15 sq. cm. do not have chronic otitis and that acute otitis does not occur if the air cell system is larger than 23 sq. cm. In normal persons the air cell system may reach a size of a little less than 30 sq. cm. If there is any obvious difference in size between the air cell systems in the two ears unilateral chronic otitis always affects the ear with the smaller cell system and unilateral acute otitis does as a rule also.—*Audrey G. Morgan.*

Calthrop, G. T. Radiological demonstration of adenoids. *Lancet*, June 1, 1940, *1*, 1005.

Occasionally, it is not possible to obtain adequate view of adenoid tissue by anterior or posterior rhinoscopy, in children. In such cases, the examiner may insert an examining finger into the posterior nasopharynx—which procedure the author believes should not be carried out on the unanesthetized child. In lieu of this, a lateral roentgenogram is recommended; the

central ray being aligned to a point 1 inch in front and 1 inch below the external auditory meatus. Large or moderate masses of adenoid tissue are easily visualized.—*A. A. de Lorimier.*

NECK AND CHEST

Muntean, Eugene, and Koch, Franz X. Das Schichtbild (Röntgen-Tomogramm) des kranken Kehlkopfes und dessen Wert bei entzündlichen und malignen Erkrankungen. (The layer picture (tomogram) of the diseased larynx and its value in inflammatory and malignant diseases.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, June, 1940, *61*, 323–337.

Progress has been made recently in the roentgenography of the larynx by the method of Réthi and Waldapfel using a small film introduced into the hypopharynx and esophagus but more particularly by the methods of tomography as described by Gunsett, Greineder and Pagani. The authors have sought to determine the value of tomography by the investigation of a large amount of clinical material.

The instrument of the Firma Sanitas was used and exposures were made at levels from 1.5–3.5 cm. below the skin contour of the Adam's apple with the pendulum swinging through an angle of 50° in a cranio-caudal direction.

The findings are described in cases of subglottic laryngitis, phlegmonous laryngitis, acute perichondritis, and peritonsillar abscess without laryngeal involvement. Several illustrations are also given of tuberculous and neoplastic involvement of the larynx. Of particular interest and importance are the inflammatory and neoplastic conditions accompanied by swelling at the entrance to the larynx. In such instances the extent of the process cannot be revealed by laryngoscopy, but is well demonstrated by tomography. The characteristic tomographic findings (Greineder) in laryngeal paralysis are described and illustrated.—*W. A. Evans, Jr.*

Colosimo, Cesare. Contributo allo studio radiologico dell' atelettasia polmonare. (Roentgen study of atelectasis of the lung.) *Radiol. med.*, Aug., 1940, *27*, 601–623.

Atelectasis means a decrease in size of the lung with great decrease or total disappearance of the air contained in it. It may be caused by obstruction of a bronchus, by primary elastic retraction of the lung or by direct pressure on the parenchyma. Cases due to the first two causes may be called ones of true atelectasis, while those due to the third cause are collapse atelectasis or, more properly speaking, collapse. The anatomical conditions are quite different in atelectasis and collapse. Really the only factor common to them is the decrease in size of the lung. But in atelectasis the decrease in size of the lung takes place first, while retraction of the wall of the thorax follows; in collapse the retraction of the wall of the thorax is primary, followed by collapse of the lung.

Atelectasis is seen in many pathological conditions of the respiratory tract, such as foreign bodies in the bronchi, tumors of the bronchi or lungs, hilar adenopathy, pleurisy, tuberculosis, pneumonia, post-diphtheritic paralysis, hemoptysis, aortic aneurysm, etc. Therefore, of course atelectasis is quite common and it is strange that it is not thought of more frequently in roentgen examination of the respiratory tract.

The following roentgen signs are seen in atelectasis of the lung: (1) uniform opacity in which more opaque cords and stripes are seen, caused by the hyperemic blood vessels. As the escape of the air from the lung is gradual the opacity does not begin immediately; (2) decrease in size of the affected lung, the margins of which are concave; this sign can be seen in the lateral projection; (3) compensatory emphysema of the non-affected areas of the lung, which often appear to be extroflexed toward the atelectatic lobe; this sign, too, must be looked for in the lateral projection, because in the frontal projection, due to the superposition of the lungs, the atelectasis is masked by the emphysema. Often the vicarious emphysema is of such a degree as to reëstablish intrathoracic equilibrium; (4) raising of the diaphragm. In extreme degrees of atelectasis there is a paradoxical movement of the diaphragm; (5) displacement and pendular movement of the diaphragm on the affected side.

Among the forms of atelectasis, that due to primary elastic retraction of the lung merits special attention, not because it has special roentgen signs different from those of atelectasis caused by obstruction of a bronchus, but because its clinical signs are so many and varied that the roentgenologist may waver a little in his diagnosis and be led to concede a doubtful or negative diagnosis. He should stand firm on his roentgen diagnosis in spite of conflicting

clinical signs if his roentgenogram shows the fundamental signs in the contracted and non-contracted parts of the lung and there are the functional signs of disturbance of intrathoracic equilibrium resembling those of bronchostenosis.—*Audrey G. Morgan.*

Westermark, Nils. On tuberculosis of bronchial lymph-glands. *Acta radiol.*, 1940, *21*, 423–442.

The commonest form of tuberculosis in children is that of the lungs and bronchial lymph glands. Nearly always in tuberculosis of the bronchial lymph glands there is a primary focus in the lung. This may be very small and difficult or impossible to demonstrate. The focus is always found in the part of the lung that is drained through the affected gland or glands. Among a group of 226 tuberculin-positive children with signs of active tuberculosis of the hilar glands a primary lung focus was demonstrated in 136 (60 per cent).

From the roentgen point of view, therefore, tuberculosis of the bronchial lymph glands may be divided into active or fresh cases and inactive or healed ones. In some cases it is impossible to state definitely whether the process is active or healed. These various groups may be subdivided into cases with parenchymatous changes and those without parenchymatous changes. The active form may be divided into cases of hilar adenitis with perihilar infiltration and those of hilar adenitis without perihilar infiltration.

Four different projections should be used in making such roentgenograms, a dorsoventral, a lateral and two oblique projections. It may sometimes be hard to differentiate between shadows produced by glands and those produced by blood vessels. In doubtful cases Valsalva's test should be made. On this experiment shadows made by arteries decrease considerably in size while those made by glands do not change. The differential diagnosis between enlarged glands caused by tuberculosis and those due to other pathological conditions is discussed.

A comparative study of the roentgen findings and the bacillary findings in 365 tuberculin-positive children showed a very good correspondence in the findings. It is possible therefore by means of a careful roentgen examination to determine the nature and extent of the process with a considerable degree of certainty.—*Audrey G. Morgan.*

Widmann, B. P., Ostrum, H. W., and Fetter, John S. Tuberculous hilar and mediastinal adenopathy in adults. *Radiology*, May, 1940, *34*, 521–529.

This article is based on 65 cases of tuberculosis of the hilar and mediastinal glands seen at the Philadelphia General Hospital in the past six years. The histories and roentgenograms of 9 of the cases are given. In 32 of the cases the conclusions were based on both roentgen and autopsy findings.

Large firm masses of glands are seen on roentgen examination but there is no absolute way of determining by roentgen examination alone whether these are caused by tuberculosis or some other disease. Final diagnosis must be based on comparative roentgen examinations and a correlation of the roentgen findings with the clinical and physical findings and the later course of the case.

In some cases the infection seems to be primary in the glands while in others there are scars of old tuberculous foci in the lungs. As a rule, there is not enough pressure to cause obstruction of the bronchi or atelectasis. There is generally no evidence of involvement of the lung until the later stages. This form of tuberculosis is most commonly found in negroes between sixteen and forty years of age and resembles the childhood form of tuberculosis. This is probably because many of this race have been infected in childhood and because they are highly susceptible to tuberculosis.

These enlarged glands may cause few symptoms or none at all in the early stages. Moderately advanced cases usually show chronic cough, with little or no expectoration, low grade fever, chest pains often described as substernal and usually intermittent fatigue, weakness, loss of weight, hoarseness, sometimes night sweats and rarely hemoptysis.

Roentgen treatment has been tried in a few cases. Small doses, 75 to 100 r, are given once or twice weekly for five or six treatments, using 200 kv. and 0.5 to 1 mm. copper filter. This treatment is well borne and may be repeated after five to six weeks if there is still enlargement. There is no evidence that this treatment has any bad effects.

In the discussion Dr. Green asked whether the mesenteric and mediastinal lymph nodes were involved and Dr. Bloom asked whether the sputum was positive and whether there was hemoptysis. Dr. Widmann replied that he was not certain in regard to the mesenteric and medi-

astinal lymph nodes. He said that many of the cases at postmortem did show involvement of the lungs with cavities, hemorrhage and sputum positive for tubercle bacilli in the terminal stages. These findings never occurred in the early stages of enlargement of the hilar and mediastinal nodes. Tuberculin tests were always strongly positive.—*Audrey G. Morgan.*

Addington, Ercell A., and Kirklin, B. R. The incidence and significance of apical lesions in pulmonary tuberculosis: a pathologic and roentgenologic study. *Radiology*, March, 1940, *34*, 327–337.

Scarring of the apices of one or both lungs is frequently seen at autopsy but little attention has been paid to it. Routine examination for this lesion has been made at autopsies at the Mayo Clinic for some years. It is a whitish opaque scar showing the picture of complete fibrosis of the apical parietal pleura. In the less severe cases the parenchyma of the lung immediately beneath it is not affected. There is some evidence in the literature that the lesion may be the focus of an adult type of tuberculous infection. A graph shows that calcification of the hilar node and apical scarring have very much the same type of curve. Apparently healed miliary tubercles of the spleen and liver are also correlated with a calcified hilar node and apical scarring.

The authors discuss the origin and mode of transmission of the infection that causes apical scarring without reaching definite conclusions. There are two normal structures at the apex the shadows of which might be confused with apical scarring, first the shadow of the subclavian artery and second that of Sibson's fascia.

This study also brings out the fact that there has apparently been a decrease in the incidence of primary tuberculous infection in the past fifteen years.—*Audrey G. Morgan.*

Gershon-Cohen, J., and Farrell, John T., Jr. The roentgenographic prognosis of pulmonary tuberculosis. *Radiology*, March, 1940, *34*, 292–299.

Though the incidence of tuberculosis is decreasing the mortality rate remains about the same. About 50 per cent of the patients who develop clinical disease die. It is therefore important for the roentgenologist to develop as accurate a method of prognosis as possible. The authors suggest a classification into benign and malignant forms and a subdivision of these into 1st, 2d, 3d and 4th stages. Descriptions are given of these forms.

Over 600 cases have been examined according to this classification and the prognoses were correct for 80 per cent. These prognoses were based entirely on roentgen findings, leaving out of account entirely the clinical and laboratory findings. A greater percentage of correct prognoses could have been made if these had been included. The best prognoses were made in the more advanced benign and malignant groups. Generally by the time roentgen examination is asked for, the disease has advanced beyond the early stage and no one, not even the roentgenologist, can make a prognosis from a single examination. Serial examinations can be made, however, and a fairly accurate prognosis arrived at in a few weeks.—*Audrey G. Morgan.*

Bagliani, Mario. Singolare comportamento di caverna tubercolare. (Unusual course of a tuberculous cavity.) *Radiol. med.*, Sept., 1940, *27*, 728–730.

A woman of thirty-five had tuberculosis of the lungs with tubercle bacilli in the sputum. Roentgen examination showed nodules of various sizes and extreme density in the right upper lobe where there was also a cavity the size of an egg with a densely opaque border. In the lower part of the cavity there was a gas-liquid level, sign of insufficient drainage. The patient could not be given collapse therapy because of diffuse adhesions with complete symphysis of the parietal pleura.

Her general condition improved with sanatorium treatment, but the cavity completely filled with fluid and showed a dense, uniform shadow. The drainage routes had evidently all been closed. In the hope of making them pervious again the patient was given roentgen treatment, 200 r, focal distance 30 cm., given in four treatments on alternate days, filter 0.5 mm. copper, 3 mm. aluminum, 150 kv.

Within the next ten days the liquid level reappeared in the cavity and direct aspiration of the cavity through the anterior wall was begun. Roentgenograms show the reduction in size of the cavity under the roentgen treatment. A direct endoscopic examination of the cavity was made. There was congestion, edema and exudation which had closed all the bronchi leading out from the cavity so that there had been no drainage. This is unusual when there are many bronchi opening into the cavity as there were in this case.—*Audrey G. Morgan.*

Sokoloff, Martin J. Lower lobe tuberculosis. *Radiology*, May, 1940, *34*, 589–594.

It was formerly believed that most tuberculosis originated in the apex and until the publication of Assmann's work in 1925 tuberculosis of the lower lobe was thought to be extremely rare. Recently, however, it has been shown that it is not uncommon. Reports of incidence by various observers vary a great deal. In the examination of 1,405 patients seen at the White Haven Sanatorium during a period of five years 24, or 1.7 per cent, were found to have tuberculosis of the lower lobe. This form of tuberculosis is seen more frequently in females than in males, the right lower lobe is affected more frequently than the left and generally the involvement is on one side only.

In almost a third of the patients the illness began suddenly with fever and the clinical picture resembled that of grippe or pneumonia. The lesions were chiefly exudative and cavities developed quickly. In some cases physical examination showed very little and it was often difficult to demonstrate tubercle bacilli in the sputum. If bacilli are not found in suspicious cases bronchoscopic examination should be made and the bronchial secretion examined for bacilli. Typical symptoms are cough, expectoration and slight daily rise of temperature, extreme fatigue, particularly in the afternoon, and light, localized night sweats. The roentgen picture is not characteristic but with these symptoms and the picture of any pathological condition in the lower lobe treatment for tuberculosis should be given.

As the condition is generally unilateral, collapse treatment is the treatment of choice. Section of the phrenic nerve is particularly valuable in this condition as the elevated half of the diaphragm presses directly on the lesion. There is some evidence that the disease is caused by tuberculin allergy, particularly in cases that begin with acute fever. In these cases violent systemic disturbance and necrosis of the lung with cavity formation are probably manifestations of a high degree of tuberculin allergy.—*Audrey G. Morgan.*

Knies, Phillip T. The significance of the roentgen visibility of the horizontal fissure. *Radiology*, March, 1940, *34*, 351–357.

Lines produced by the horizontal fissure of the right lung appear in the roentgenograms of about 20 per cent of normal cases. Effusions in the pulmonary fissures have sometimes been attributed to unresolved pneumonias. But while such lines do appear in about one-fifth of normal cases they appear in twice as many cases with pulmonary tuberculosis and in three times as many cases with heart disease. This shows that they are often pathologic in nature. Very heavy lines are rarely seen in normal cases and almost always indicate some pathological condition. The visibility of the horizontal fissure is often caused by a thickening of the film of interlobar pleural fluid due to hydrothorax. This is frequently so slight in degree that it cannot be detected in any other way. Visibility of the lines may also be caused, in some cases by inflammatory pleural and subpleural condensations. The fissure is visible in cases with enlarged heart, no matter what the type of heart disease, and seems to be related particularly to the degree of decompensation.

The importance of such visible pleural lines must be determined in each individual case; they cannot always be attributed to pathological conditions as they appear in such a considerable percentage of normal chest roentgenograms.—*Audrey G. Morgan.*

Fossati, Franco. Voluminosa raccolta idroaerea della grande scissura interlobare destra. (Large accumulation of gas and liquid in the great interlobar incisure on the right side.) *Radiol. med.*, Sept., 1940, *27*, 727–728.

A young man of eighteen who for some time had had cough with scanty expectoration, poor general condition and slight fever was sent for treatment for a basilar pleurisy on the right side which had been confirmed by exploratory puncture by the attending physician. Roentgen examination in addition to a slight basilar effusion on both sides showed a large accumulation of gas and liquid the size of the head of a fetus, oval in shape, in the middle of the right half of the thorax. The liquid level changed with change in position of the patient. In the lateral projection the liquid seemed to be almost in the central plane.

In addition to this there was a density of the lung parenchyma in the right subclavicular region, bronchopneumonic in type, which was later explained by the finding of tubercle bacilli in the expectoration.

Differential diagnosis had to be made between an accumulation of gas and liquid in the great interlobar incisure, a pulmonary abscess,

large tuberculous cavity or a large echinococcus cyst communicating with a bronchus. The latter was excluded by the septic fever and the positive Koch's bacillus and negative Casoni tests and the lack of any history of infection. Abscess of the lung was excluded by the unusual size of the shadow, the scanty expectoration and the absence of fetor ex ore. It did not seem probable that it was a large tuberculous cavity opening into a bronchus because of the lack of objective signs of a cavity opening externally, the brevity of the illness, the large amount and mobility of the liquid contents, the regularity of the outline and the size of the shadow, which in the lateral projection seemed to pass beyond the boundary of a single lobe. The presence of tubercle bacilli in the sputum, which might seem to confirm the above theory, was explained by the infiltration in the right upper lobe. Therefore the diagnosis of a large collection of gas and liquid in the right interlobar fissure was made and confirmed by exploratory puncture with the withdrawal of 40 cc. seropurulent fluid. The patient made a complete recovery.—*Audrey G. Morgan.*

Evans, E. E. An x-ray study of the effects of industrial gases upon the human lung. *Radiology*, April, 1940, *34*, 411–424.

The author who is the Medical Superintendent of the Dye Works of the E. I. du Pont de Nemours and Co., Inc. of Deepwater, N. J. has for five years been engaged in a roentgen study of the lungs of workmen exposed to low concentrations of various gases, including hydroflouric acid, chlorine, hydrochloric acid, sulfur dioxide, sulfur trioxide, phosgene, phosphorus oxychloride and phosphorus trichloride. The average age of the men in this plant is 39.25 years and the average service 8.3 years. The total number of employes is 3,798.

Serial roentgenograms were made during the five year period with the standard technique. About 17,000 roentgenograms were made. Forty of them are reproduced and brief discussions given of the cases represented.

On admission these men had some changes in the lungs, such as fibrosis or fibrosis and calcification, indicating healed tuberculosis. During the five years' exposure to the gases named above no visible changes took place in the lung tissue. During the five years clinical studies of the men were also made and there was no higher death rate from pneumonia and other lung infections than among the other workmen in the plant not exposed to these gases. Serial films of the lungs of other employe groups showed similar pictures. The work will be continued but the author's impression is that with present methods of operation these men are not exposed to any danger from the gases.—*Audrey G. Morgan.*

Hodges, Fred Jenner. Differential diagnosis of non-specific interstitial pneumonitis. *Radiology*, March, 1940, *34*, 276–282.

Pneumonitis and pneumonia both mean inflammation of the lung. But it has become customary for pathologists to use the term pneumonitis for an inflammation of the chronic interstitial fibroid type which is quite different from an actue pneumonia. It is not always possible to determine the cause of such a chronic pneumonitis. Cases are described and illustrated which show lesions due to silicosis, syphilitic infection, actinomycosis, tumor metastases and repeated large doses of roentgen radiation. It often requires the combined methods of physical diagnosis, radiology, pathology, bacteriology and serology to demonstrate the true cause of the disease. The name chronic nonspecific interstitial pneumonitis can be used by the roentgenologist to indicate that he has found evidence of longstanding inflammation of the lung but that he is not able to determine its exact cause.—*Audrey G. Morgan.*

Doub, Howard P. The roentgenologic aspects of bronchomycosis. *Radiology*, March, 1940, *34*, 267–275.

Both the clinical and roentgen signs of bronchomycosis are very much like those of tuberculosis and even the complications may be the same. The final diagnosis must be based on the discovery and identification of the causative microorganisms. Norris reports yeasts in the sputum of 15 per cent of the patients in a tuberculosis sanatorium. This does not necessarily mean primary fungus infection but in all such cases careful examinations should be made to determine what is the primary infection.

Four cases of bronchomycoses are described and illustrated with roentgenograms. The roentgen picture of the different forms of mycoses is discussed. There are no characteristic changes that makes it possible to differentiate these mycoses definitely from each other and from tuberculosis. Associated lesions outside the lungs, such as bone lesions, fistulae and granulomatous skin lesions may help in making

the diagnosis. Miliary nodules are found in some form or other in all the mycoses except actinomycosis and aspergillosis. Im blastomycosis there is usually more fibrosis than in tuberculosis. In some cases of moniliasis there is studding along the bronchi and nodules which are generally larger and less discrete than those of tuberculosis. Necrosis of the lung with abscess formation is seen at some stage of the disease in a number of these infections. It may extend to the chest wall and lead to the formation of persistent fistulae. Involvement of the pleura with or without empyema may be seen in any of these infections and is often a prominent feature of actinomycosis. Sometimes involvement of the base is more prominent than that of the apex, which is a differential sign from tuberculosis.—*Audrey G. Morgan.*

Hartung, Adolph. Pulmonary involvement in the lymphoblastomas: special reference to roentgen aspects. *Radiology*, March, 1940, *34*, 311–316.

The name lymphoblastoma has been applied to many conditions. In this paper only Hodgkin's disease, lymphosarcoma and chronic lymphatic leukemia are considered. The roentgen findings in these three conditions are enough alike so that they may be grouped as a unit. Statistics indicate a rather high percentage of lung involvement in these cases.

This paper is based on 35 cases, 24 of Hodgkin's disease, 6 of lymphosarcoma and 5 of chronic lymphatic leukemia. During the period in which they were seen 130 cases of lymphoblastoma confirmed by biopsy were reported. This would indicate that slightly less than 50 per cent of the lymphoblastomas had intrathoracic involvement and in 25 per cent the lungs were affected. The roentgen findings are more or less like those of other chronic or slowly developing lung lesions. The most accurate way of diagnosing lung lesions of lymphoblastomatous origin is by biopsy, though regression under irradiation is almost as conclusive.

As to radiation treatment of these lesions it has been claimed that they are more radioresistant than superficial nodes, but the author has not found this to be true. In the 26 cases of this series that were given roentgen treatment 16 showed well marked regression. Four of the 6 cases of lymphosarcoma were irradiated and all of them showed regression. Of the 5 cases of lymphatic leukemia 3 were irradiated but only 1 showed well-defined regression of the lung lesions.

If all cases in which the lesions are apparently limited to the superficial nodes were examined carefully many more cases of involvement of the lung parenchyma would be discovered.

In the discussion of this paper Dr. Grier said that he would be inclined to separate lymphosarcoma from leukemia and Hodgkin's disease because he always expects to find involvement of the lung in lymphosarcoma but not in the other two conditions. He has thought that involvement of the lung, especially in Hodgkin's disease, occurrred only in the terminal stage. Obviously from Dr. Hartung's findings examination of the chest should be made at once in cases of Hodgkin's disease and leukemia. He refers to actual invasion of the lung tissue, not merely of the glands in the mediastinum or the hilum. Everyone expects the gland involvement. He is inclined to agree with Dr. Hartung that the parenchymatous lesions are as radiosensitive as the superficial lesions.

Dr. Harrison of London said that this paper reminded him of an experiment that he had made in Zürich under Prof. Schinz. They collected the material of mediastinal tumors in the Canton Hospital and after excluding as far as possible the cases of Hodgkin's disease, tuberculosis and thymoma, 36 cases of lymphoblastomatous tumors remained. These showed blood changes ranging from that of a frank, serious leukemia to cases with no blood changes at all. There were 6 of these. All of the patients except 2 or 3, who were too moribund, were irradiated. All with fairly marked lymphatic leukemia improved at first but soon relapsed and died following the usual course of lymphatic leukemia. Among the 6 cases with no blood changes, diagnosed as lymphosarcoma, without biopsy, 3 showed no response and soon died. The other 3 cleared up. That is, the only 3 among the 36 that cleared up were ones with no blood changes. He asked Dr. Hartung whether he had found that the mediastinal tumors without blood changes responded most favorably to irradiation.

Dr. Hartung replied that of course the prognosis is bad in practically all cases of lymphoblastoma. But in one of his cases followed for nine years the patient survived five years after the lungs became involved. He could give no figures in regard to the blood findings in the cases of lymphatic leukemia but most of them showed no regression under irradiation.—*Audrey G. Morgan.*

Møller, P. Flemming. Some words on the silicosis problem. *Acta radiol.*, 1940, *21*, 571–576.

For many years silicosis has been considered a serious problem in mining districts. It is not so well known, however, that it occurs in some other dust-producing industries to a greater degree than in mining.

The nature of the dust inhaled has a great deal to do with the roentgen picture in silicosis. The type of the disease also depends to a great extent on the amount of dust inhaled by the worker. For example, there is a great deal of silicosis among the granite quarriers in England and America and the disease develops very rapidly, while in the quarries in Denmark there is little silicosis and it develops slowly. The granite workers in Denmark work largely in the open air.

Tuberculosis is generally believed to be the most frequent and serious of the complications of silicosis, but the author does not believe that this is true. In Denmark investigation has not shown that tuberculosis is particularly frequent or particularly severe in silicosis. Many cases of silicosis are mistaken for old tuberculosis on the basis of the roentgen examination because the examiners do not know that a silicosis in the third stage may look just like a case of old tuberculosis. Some authors even say that massive silicosis is always complicated by tuberculosis, but the author does not believe that this is true. He presents two roentgenograms of a case in support of this contention. Clinically there was nothing to indicate that this man had tuberculosis and when he died of pneumonia, autopsy did not show fresh tuberculosis. This picture, with many calcifications, shows that a silicotic lung is really not a very favorable field for the development of tuberculosis.

If fresh tuberculosis is found in a silicotic lung fairly isolated from the silicotic process, it is not hard to differentiate between the silicotic and tuberculous processes. But if they blend it may be impossible to make a diagnosis from the roentgenogram alone; the history and clinical signs must be considered too.

The author has never seen cavities in roentgenograms of uncomplicated silicosis, though he has sometimes seen them on autopsy. Localized emphysematous areas with large emphysema bubbles may simulate tuberculous cavities. Emphysema is one of the chief complications in severe cases of silicosis. This of course not infrequently results in spontaneous pneumothorax. Roentgenograms are shown of one such case during life and after death.

Another danger in silicosis is hypertrophy of the heart, resulting in degeneration of that organ. There is danger of sudden death in silicosis at any time from spontaneous pneumothorax or paralysis of the heart. There is also danger of complicating lung diseases and they are particularly serious because so large a part of the functioning lung tissue has been destroyed.

The patient's general condition is often not nearly as serious as the roentgenogram would indicate but there is always this danger of sudden death from complications. In the author's study of 798 porcelain workers in 1932 there were 18 patients with third degree silicosis. Five years later 8 of these patients were dead, 7 of them from respiratory diseases.—*Audrey G. Morgan.*

Pendergrass, Eugene P., and Hodes, Philip J. The modifying influences of silicosis and silicosis with infection upon the healthy chest. *Radiology*, April, 1940, *34*, 400–404.

Roentgen examination is the best method of determining the changes brought about in the lungs in silicosis, and pneumoconiosis in general. The roentgenologist therefore who works in these diseases must be thoroughly familiar with the normal lung pictures, the roentgen appearance of pneumoconiosis and conditions simulating it and the proper technique for obtaining the best films.

Silicosis may be simple or complicated by infection. In simple silicosis small discrete nodules of fibrous tissue are scattered through both lungs. Conglomerate shadows may develop from a combination or coalescence of discrete nodules. The part of the lung in which conglomeration develops may have been injured previously by a local inflammation. More dust would tend to collect in such an area, forming a conglomerate shadow.

During the active period of some infections the lesion extends to the periphery of the lung in many cases. Massive shadows of homogeneous density are characteristic of advanced silicosis with infection. Usually the architecture of the lung is entirely obliterated and it requires overexposed films to penetrate the dense shadow and analyze the internal structure. The only safe way to determine the activity of a silicotic process is to make serial examinations.

It has long been thought that silicosis is necessarily progressive and fatal. But increasing

experience with workers in silica has shown that the prognosis is not so hopeless as was thought. If factors which cause further fibrosis, such as additional silica, congestion and infection can be avoided patients with slight fibrosis may remain well. But if acute or chronic infections occur little can be done to prevent massive fibrosis. The important thing to do is to limit the hazard as much as possible in stabilized cases and to remove from the industry men who have active infection. If taken away from the work and properly treated these men may be cured.—*Audrey G. Morgan.*

Douglas, Bruce H., and Tompkins, Edmund. Silico-tuberculosis as seen in a large industrial center. *Radiology*, April, 1940, *34*, 405–410.

The authors report 134 cases of silicotuberculosis seen in the Tuberculosis Division of the Herman Kiefer Hospital in Detroit. There are many dust hazards in this industrial community. The majority of these patients were foundry workers.

There is no treatment for uncomplicated silicosis and even after exposure to dust has been stopped it is generally progressive. The prognosis of silicotuberculosis is even worse than that of either of the diseases alone. Of the 31 cases diagnosed during the first year of this study (1933) 87.1 per cent were dead by the end of the five year period and 58.3 per cent of the total 132 cases were dead. Among 205 cases of bilateral tuberculosis without silicosis only 25.6 per cent were dead after seven years. Collapse treatment, which is so effective in uncomplicated tuberculosis, is contraindicated in silicotuberculosis. Among 21 cases given collapse treatment only 2 have done well and sometimes the condition is aggravated. This leaves only rest in bed as a method of treatment and this only prolongs life somewhat but does not arrest the disease.

Therefore it is extremely important to diagnose silicotuberculosis accurately for if the patient with silicosis without tuberculosis is put in a hospital for tuberculosis he may contract the disease. The patient with uncomplicated silicosis does not need rest in bed but should be kept as active as he is physically able to be. The patient with tuberculosis without silicosis should have the latter condition ruled out as quickly as possible so that collapse therapy may be given.—*Audrey G. Morgan.*

Zuckerman, S. Experimental study of blast injuries to the lungs. *Lancet*, Aug. 24, 1940, *2*, 219–224.

The effects of blasts (compression and suction waves) were studied experimentally on mice, rats, guinea pigs, rabbits, cats, monkeys and pigeons. The animals were placed at distances of 13 to 18 or more feet from the site of explosions. At these distances the hydrostatic pressures varied between 126 and 62 pounds per square inch and practically all animals were killed. Yet there were no external signs of injury. Autopsy studies revealed the outstanding lesion to be bilateral pulmonary hemorrhages.

With distances greater than 18 feet (i.e. with less hydrostatic pressure than 62 pounds per square inch), no animals were killed, though some showed irregularity of breathing and blood in the upper respiratory passages.

Autopsies performed on animals which survived the explosions showed some petechial hemorrhages beneath the pleurae, especially along the rib contact surfaces. Lacerations were found in some instances with resultant pneumothorax or hemothorax. Cases of internal hemorrhage usually showed related lung surface hemorrhage. The most vulnerable region appeared to be the anterior and basal portions. All cases which died showed blood stained fluid in the trachea and bronchi. Microscopically, ruptured capillaries were demonstrated in the alveoli. Interstitial hemorrhages also occurred. Though sufficient evidence is not yet available, it appears that larger animals are not as vulnerable as smaller ones.

The author is of the opinion that these lesions are produced during the pressure wave because of the severe degree of impact. It is estimated that the compression wave endures for about 0.006 second; the suction wave, for about 0.03 second. The suction component is much weaker than the pressure component since it can be no greater than 15 pounds per square inch (as in the case of a perfect vacuum).

Roentgenologically, there may be evidence of alveolar hemorrhages.

Thus, in the case of a bomb explosion, one may be wounded by: (*a*) impact of fragments—bomb or masonry; (*b*) being violently thrown and suffering an impact when striking another object; (*c*) being affected by the blast wave. This last type of injury was mentioned during World War I; it was reported in the Spanish War and now, on the basis of experimental

studies—in all of which blood stained fluid was found in the mouth and nose of the victims.—*A. A. de Lorimier.*

Dean, D. M., Thomas, A. Robinson, and Allison, R. S. Effects of high-explosive blast on the lungs. *Lancet*, Aug. 24, 1940, *2*, 224–226.

Reference is made to a circular letter from the Ministry of Health wherein warnings were given that severe chest injuries might occur after blasts of high explosive bombs, without evidence of any external wounds.

The authors have abstracted the findings in 27 cases which had been in close proximity to such blasts. Twenty-one had extensive superficial burns; 5 had fractures; 1, splinter wounds of the legs; 7 had suffered concussion by the explosions; 3 had been immersed in the sea and all but 2 had been subjected to the effects of direct exposure to the blasts, at close quarters. The observations were made nine to ten days following the explosions.

Cough and expectoration were noted by 6 patients (dyspnea and restlessness in 1 case). These symptoms were noted between the second and the fifth day—in no case, on the day of the bombing. None of them had complained of pain in the chest nor of hemoptysis.

Abnormal physical findings were noted in 16 cases. These included: fullness, lower portions of the thorax (15 cases); diminished diaphragmatic movements (10 cases); generalized hyperresonance (1 case); impaired resonance at one or both bases (3 cases); loud harsh breath sounds (1 case); faint breath sounds (7 cases), and crepitation (6 cases).

Abnormal roentgen findings were noted in 14 cases. These included: consolidation of a portion of a lung (lower lobe, 1 case); congestive changes as seen in bronchopneumonia (1 case) and criteria of pleural thickenings (slight increase in tissue density and limitation of rib expansion, 12 cases).—*A. A. de Lorimier.*

Taussig, Helen B., and Goldenberg, Marcel. Roentgenologic studies of the size of the heart in childhood. I. Three different types of teleroentgenographic changes which occur in acute rheumatic fever. *Am. Heart J.*, April, 1941, *21*, 440–469.

Three groups of cases are described: one in which the heart remained within normal limits of size in spite of valvular lesions, another where the heart enlarged and then remained stationary in size while the chest grew, and a third group where there was progressive cardiac enlargement. The study was based on teleroentgenograms in the frontal plane with measurement of the cardiothoracic ratio. The 44 cases in the first group where there was normal growth of the heart relative to the chest include 30 who had multiple attacks of rheumatic fever and never gave any clinical evidence of permanent myocardial or valvular damage, and also 14 who showed evidence of permanent valvular damage without cardiac enlargement. The prognosis is good in this group and there was only one fatality which occurred during a recurrent attack of acute rheumatic fever.

The cases of the second group showed cardiac enlargement when first seen, but this was not progressive and with the increase in the size of the chest incident to growth the cardiothoracic ratio decreased often to average normal valves. This phenomenon was observed in 24 cases, 5 with no demonstrable valvular damage, 6 with mitral insufficiency, 6 with mitral insufficiency and stenosis, 3 with aortic insufficiency and 3 with multiple involvement. In these cases the course of the disease was remarkably satisfactory; there were 3 deaths, 2 from subacute bacterial endocarditis and 1 from acute rheumatic fever.

In the third group there was a progressive increase in the cardiothoracic ratio. From six months to five years were required for the enlargement to develop. The type and severity of the valvular lesions were comparable to the preceding group. In this group the prognosis was very poor; the mortality rate was 50 per cent, and 25 per cent were chronic invalids. The remainder have had repeated attacks of rheumatic fever or have shown laboratory evidence of a persistently active infection.—*W. A. Evans, Jr.*

Evans, John R., and Bouslog, John S. Intractable heartburn of pregnancy. *Radiology*, May, 1940, *34*, 530–535.

Intermittent heartburn is not unusual in pregnancy but in some cases the heartburn persists and becomes progressively worse until after delivery when it stops entirely. Some years ago Evans discovered accidentally in making a roentgenogram in such a case that it was caused by a hernia of the esophageal opening. This same cause has been found in all similar cases examined since. Four cases are described and

roentgenograms and diagrammatic drawings of the condition during pregnancy and after delivery given. No treatment has proved effective. —*Audrey G. Morgan.*

Potter, Hollis E., Douglas, Bruce H., and Birkelo, Carl C. The miniature x-ray chest film. *Radiology*, March, 1940, *34*, 283–291.

Several plans for photographing the screen image of the chest have been developed for the purpose of examining large numbers of persons for tuberculosis. The authors have worked out a method of making a 4×5 inch film. A modern roentgen machine is used with a rotating anode tube capable of handling 400 ma. of current at from 60 to 80 kv., an impulse-timer and a tube-screen distance of 50 inches, or 125 cm., which produces as little distortion as possible. The exposure time varies from 1/20 to 4/20 second, depending on the thickness of the chest. The screen used is nearly 7 times as fast as the usual Patterson screen. The lens used, with a rating of F 1.5 is capable of producing a sharp image in an area 3.7 inches in diameter on the 4×5 inch film. For the best results the patient's chest image must be within this area and therefore carefully centered.

The authors used this method in examining 1,610 persons and compared the results with those of the regular 14×17 inch film, both being taken at the same visit of the patient.

They found the 4×5 inch photoroentgenogram quite accurate. There was only 2.6 per cent error in detecting the 271 positive cases among the 1,610 persons examined. The method can be applied rapidly and economically in the examination of large number of persons, slightly faster than one per minute with a considerable reduction in cost. It has definite advantages over other roentgen methods of examination either in accuracy or cost or both. It can be applied accurately and economically without preliminary tuberculin testing.—*Audrey G. Morgan.*

Robins, Arthur B., and Ehrlich, David E. Group x-ray surveys in apparently healthy individuals. *Radiology*, May, 1940, *34*, 595–609.

The authors, who are respectively Supervisor of Clinics and Supervising Roentgenologist, Bureau of Tuberculosis, Department of Health, New York City, say that effective control of tuberculosis must be based on a sound case-finding program. Formerly in the New York Department of Health they examined all persons suspected of having tuberculosis and all patients admitted to hospitals. But this did not uncover the early cases with minimal lesions and patients must be discovered in this early stage, not only for the sake of their cure but for the sake of preventing them from spreading the disease.

In 1933 they first had an opportunity to examine 20,000 apparently healthy individuals on home relief in New York City. Since then they have had an opportunity to examine other groups in high schools, prisons and city employees, a total of more than 73,000 persons. Tables are given showing the incidence of tuberculosis in the different groups, classified according to age, sex, color, etc. They considered various methods of examination including tuberculin test screening, fluoroscopy, roentgen examination on celluloid film and the rapid roll-paper method. They decided in favor of the latter.

They conclude that this method of detecting tuberculosis in apparently healthy individuals should be a part of the program of all large public health organizations. The greater part of the effort should be expended on adults and persons at low economic levels. The incidence of tuberculosis in Negroes is lower than in whites among the apparently healthy population. Most of the cases are discovered in the minimal stage when treatment is most effective. Evidence of heart disease was found in a large enough percentage of the cases to justify roentgen examination of the whole population.

They found the roll-paper method the best one from the point of view of convenience, accuracy and economy in the rapid examination of large groups.—*Audrey G. Morgan.*

Tice, Frederick. The miniature x-ray film in the "total survey." *J. Am. M. Ass.*, Oct. 12, 1940, *115*, 1254–1257.

The necessity for a "total x-ray survey" in certain areas of high mortality in Chicago has long been realized. By total survey is meant survey, in the district selected, of every man, woman and child, reaching toward an ideal, though probably unobtainable, objective of 100 per cent.

A roentgen-ray project of the magnitude indicated was impossible because of expense until the advent of roentgen photography. In the

work being reported here the photoroentgenographic unit developed by one of the equipment houses in collaboration with Potter, reported elsewhere by Potter and Douglas, was used throughout. The size of the film is 4 by 5 inches and the approximate cost of each film is 5 cents.

To avoid individualistic trends, the films were read by a committee of four head physicians, all especially experienced in roentgen interpretation. Opinion had to be unanimous on every diagnosed case. All films showing suspicious or abnormal markings were classed as suspects and followed up by a large film examination. With regard to the technique of film examination, a double cone-shaped box 22 inches long with a 4 inch magnifying glass at the anterior apex was devised. A runner 30 inches long, capable of holding 6 miniatures, is part of the equipment. The magnified image is about 8 by 10 inches, is easy on the eyes and shows a fine differentiation of detail.

In a two months' survey, 9,348 persons were roentgenographed and classified, of whom 351 showed roentgenologic evidence of tuberculosis on the original miniatures. One hundred and sixty-seven were minimal, 141 moderately advanced and 43 far advanced. In addition, 45 cases were read as suspects on the original miniature and diagnosed as tuberculosis on later 14 by 17 inch films. The 340 white persons roentgenographed showed a higher rate of incidence than the 8,942 Negroes. An unusually high rate was found in children.—*S. G. Henderson.*

Heaf, Frederick. Mass radiography in practice. *Lancet*, Nov. 16, 1940, *2*, 611–612.

This article is a plea that embarrassment be not imposed upon those in whom roentgen findings of tuberculous lesions are reported. The author emphasizes that though mass roentgenography serves to discover cases of pulmonary tuberculosis, nevertheless it should be considered mainly as an examination for general fitness. Negative findings should not lead one to ignore symptoms which might later develop; positive findings may not necessarily indicate a state of actual invalidism.

The literature suggests that about 1.5 per cent of those examined will be found to be suffering from active pulmonary tuberculous lesions while perhaps 4 per cent will show abnormal shadows.

Roentgen findings may be due to: (1) Active lesions—most of which will require sanatorium care. As soon as possible these cases should be usefully employed under medical supervision. (2) Latent lesions—though symptomless, the character of their roentgenographic shadows indicating infiltrates which may increase at any time and produce symptoms. (3) Early quiescent lesions—having the background of symptoms but showing indefinite or very slight roentgenographic evidence. (4) Advanced quiescent lesions—having the background of symptoms with definite roentgenographic evidence.

Cases of Group (1) should be notified of their condition and they should be hospitalized in order to receive adequate treatment. Cases of Groups (2) and (3) should not be notified nor hospitalized though repeated study should be made of them. Moreover, they should be insured of proper nourishment and suitable employment. Cases of Group (4) are likely to break down. They should be given medical supervision and sheltered conditions of employment—such as are to be found in a village settlement.

Supervision of these cases should be conducted by social welfare workers, not by the staff of a tuberculosis dispensary. The roentgen findings in the case of an apparently healthy individual should not be divulged except to the extent of rendering professional information, after a group of three doctors have reached a unanimous decision as to the diagnosis. This is particularly important when dealing with insurance companies. Approximately 25 per cent of lesions which are roentgenographically classified as "abnormal" eventually manifest activity.—*A. A. de Lorimier.*

McGibbon, John E. G. Cinebronchography (cinematography through the bronchoscope). *Lancet*, June 15, 1940, *1*, 1083.

The author has developed apparatus for accomplishing motion photography not only of the larynx but also of the trachea and larger bronchi, thereby providing views of the walls and also changes incident to various movements —respiratory, cardiac and coughing.

The apparatus consists of a lens assembly, a bronchoscope, a camera unit and provision for special lighting.

The lens has a focal length of 10.5 cm. and an effective diameter of 7.0 mm. It is mounted in a tube which has an external diameter of 10.0 mm. and a length of 12.1 cm. At one end of this tube there is an adaptor for the camera.

The bronchoscope is 40 cm. long and has an external diameter of 11.0 mm. plus an alternate air passage along its upper 9 cm. and an accessory tubing for special lighting. The lighting is provided by two bulbs operated at 4.4 v. and a wattage of 1.25.

The camera is an f 1.9 Cine Kodak. Super X Cine Kodak film is used, run at a speed of twenty-six frames per second. The area that can be photographed is less than 1.5 cm. from the tip of the bronchoscope. The bronchoscope should be rotated during the exposure in order to provide for variations in light reflex.—*A. A. de Lorimier.*

ABDOMEN

Ascroft, P. B., and Samuel, Eric. Radiography in postoperative ileus. *Lancet*, Oct. 12, 1940, *2*, 445–449.

A clinical diagnosis of intestinal obstruction is easily decided in the case of a fit individual who is suddenly stricken with intestinal colic, vomiting, absolute constipation and distention. When this syndrome is not so complete, roentgenological studies may be indicated. These studies should be made without the use of barium. The roentgen evidence might include accumulations of gas and possibly fluid levels.

Postoperatively, the recognition of obstruction is more difficult. Whenever the abdomen is open, motility, secretory and absorptive activities may be physiologically inhibited for some hours—usually six to twelve. Two types of obstruction may occur: "focal" or "diffuse." Focal obstruction is usually located at the site of sutures while diffuse obstruction is more widespread and results because of infection.

The results of 19 such cases are cited and much discussion is given to the mechanics concerned.

The author emphasizes the thought that if roentgenography reveals distention of the colon alone, passage of a flatus tube is indicated; if feces are conspicuous, an enema is indicated; if the small bowel is distended so that there are fluid levels, no food and little or no fluid should be taken. If improvement is not rapid, the stomach should be continuously aspirated. Serial roentgenograms should be obtained. Suction may result in rapid clinical improvement even though the obstruction itself be not eliminated. If ordinary roentgenograms do not present evidence of the disappearance of obstruction, a small quantity of barium may be injected by means of the tube (Miller-Abbott); if it does not pass the obstruction, it should be aspirated.—*A. A. de Lorimier.*

Hultén, O. Über den Nutzen von Röntgendiagnostik bei akuten Bauchfällen. (The value of roentgen diagnosis in acute abdominal cases.) *Acta radiol.*, 1940, *21*, 471–482.

This article stresses the importance of collaboration between surgeon and roentgenologist. The surgeon should, if possible, be present at the roentgen examination and should evaluate the roentgenograms together with the roentgenologist. Close personal cooperation between the two is essential for good results. In this special field of diagnosis serial roentgenograms of acute cases may be necessary.

Roentgen examination has been used for a long time in the diagnosis of certain acute abdominal cases, such as ulcer, ileus, colic from ureteral stones, etc. But in Upsala it is used very freely in the diagnosis of all acute abdominal cases. The author has collected a material of several thousand cases. It is of special value in reducing the necessity for exploratory laparotomies.

The commonest form of acute abdominal disease is acute appendicitis. This shows an abscess shadow and sometimes around it dilated loops of small intestine with a fluid level. Roentgen examination is particularly valuable in appendicitis in children, in whom the clinical findings are not always clear; it is also most valuable when the appendix lies in an abnormal position. Roentgen examination is also valuable in peritonitis and in residual abscesses after peritonitis. Pus can generally be shown earlier by roentgen examination than by palpation. One note of warning is necessary. The shadow persists for some time after the abscess has been opened and drained. Such an old abscess shadow may be interpreted as the cause of disease which is in reality caused by pus localized somewhere else. Subphrenic abscess can also be diagnosed by roentgen examination, though not always in the very beginning. The value of roentgen examination in the various forms of ileus is very well known. Ileus can be diagnosed even in the very first stages by giving 1 to 2 tablespoonfuls of barium by mouth. Differentiation can be made between ileus of the small and large intestine by giving a barium enema. The author thinks it is almost always permissible to give a small amount of barium by mouth, even

though there may be perforation of the intestine.

In acute pancreatitis the duodenum is often dilated and paretic. Perforation of gallstones from the gallbladder into the duodenum causes the picture of acute stenosis of the pylorus. From the duodenum the stones may pass upward into the stomach or downward into the intestine. A differentiation between appendicitis and stone in the right ureter may be made by roentgen examination. It is also of value in perinephritis.

In traumatic injuries of the abdomen roentgen examination shows gas or blood in the abdomen. Roentgen examination promises to be of great value in war surgery. Because of the danger in transporting abdominal cases it will be necessary to have the roentgen installation very close to the front and for the cooperation between surgeon and roentgenologist to be even closer than in civil surgery.

Great caution should be exercised in interpreting negative roentgen findings.—*Audrey G. Morgan.*

Inlow, Herbert H. Shellac bezoars. *Radiology*, May, 1940, *34*, 618–625.

A case is described in a man, aged thirty-three, who worked in a factory where mirrors were made. He came for treatment on account of symptoms resembling those of peptic ulcer. Roentgen examination showed eventration of the diaphragm, with malposition of the heart and stomach, gastric ulcer and a mass which proved to be a bezoar. The latter was removed and he made an uneventful recovery.

He had not swallowed any indigestible substances such as hair or persimmons. The surface of the mass looked like varnish and chemical examination showed that it contained shellac. It was found that in the factory a coating of shellac was put on the backs of the mirrors. The patient, as well as some of the other workmen, had used the shellac as an intoxicant. The shellac was added to a glass of dry beer which was stirred in order to precipitate most of the shellac. The small amount of shellac retained was eliminated promptly by the normal stomach but the patient's stomach was so situated that it retained the shellac and formed a bezoar.

These shellac bezoars are extremely rare, this being the eleventh case described. All the cases were in male drunkards who drank shellac solution.—*Audrey G. Morgan.*

McPeak, Clarence N. Benign duodeno-colic fistula. *Radiology*, March, 1940, *34*, 343–350.

Duodenocolic fistula is rare. If malignant it is generally caused by carcinoma of the colon, if benign by perforation of duodenal ulcer into the transverse colon. The patient may or may not have sudden pain when the ulcer perforates. A history of persistent diarrhea with rapid loss of weight in spite of voracious appetite is quite typical of the condition. The author briefly reviews 2 cases from the literature in one of which the fistula was diagnosed by roentgen examination but not operated on and in the other it was not diagnosed on roentgen examination but on operation.

The best method of examining for duodenocolic fistula is with a barium enema. Negative results from a barium meal do not necessarily disprove its existence.

In the author's 2 cases the fistula was diagnosed by roentgen examination and confirmed by operation and in the second case by autopsy. The patient died of an abscess that developed after the operation. The first patient made a prompt and complete recovery. In both these cases the fistula was benign. Definite differentiation between benign and malignant processes cannot be made by roentgen examination but this is not necessary as operation must be performed in either case.

In the discussion Dr. Camp said that no such cases due to perforated duodenal ulcer had been seen in the Mayo Clinic. He thinks there was rather definite clinical evidence in Dr. McPeak's cases that the condition was benign. Both patients had a history of duodenal ulcer complicated by a sudden attack of pain. This is not usual in malignant disease. It is important to make the differentiation if possible as the finding of a benign lesion justifies radical surgery.—*Audrey G. Morgan.*

Perotti, Desiderio. Invisibilità di ulcere gastro-duodenali al primo pasto opaco—visualizzazione della nicchie ad un secondo pasto immediatamente susseguente. (Invisibility of gastroduodenal ulcers on a first opaque meal—visibility of the niches on a second opaque meal given immediately afterward.) *Radiol. med.*, Aug., 1940, *27*, 645–648.

Two cases are described in which the patients showed symptoms of gastroduodenal ulcer. One was a man of fifty and the other a man of fifty-five. On the first examination both showed re-

gional spasms and rapid and irregular peristalsis. No niche was visible on the roentgenogram taken with the patient standing after the first roentgen meal. Roentgenograms were then taken, in both cases, with the patients lying down. During the taking and development of these roentgenograms all the opaque paste had passed into the intestine. In each case a second roentgenogram was then taken with the patient standing and in both cases the niche could be seen clearly.

The factors that made the author decide to take the second roentgenograms in these cases was the hypertonicity of the stomach on the first examination, the irregular peristalsis, the signs of localized spasm and the rapid emptying. When the muscles of the stomach relaxed the margins of the ulcer crater opened a little and allowed the opaque material to enter the niche, so that it showed on the roentgenogram.

If there are clinical signs of ulcer and an indirect roentgen syndrome, the roentgen examinations should be repeated, using all sorts of technical maneuvers in an attempt to demonstrate the niche.—*Audrey G. Morgan.*

Hatchette, Stakely. Multiple diverticula of the jejunum, duodenum and colon. *Radiology*, May, 1940, *34*, 577–580.

Diverticula of the jejunum are very rare. The author describes a case in a woman fifty-three years of age who came for examination because of nausea, colicky pain in the epigastrium, indigestion and occasional attacks of vomiting. There was no difficulty in making the diagnosis of diverticula as when the progress of the barium meal was observed under the fluoroscope the filling of the diverticula could be seen readily and their relationship to the other parts of the digestive tract noted. The twenty-four hour roentgenogram showed the multiple diverticula of the colon. The roentgenograms are given.

There were no signs of carcinoma in the chest, though she had been irradiated six years previously for a Grade 4 adenocarcinoma of the left breast.—*Audrey G. Morgan.*

Jenkinson, E. L., and Waskow, W. L. Polyps of the large bowel. *Radiology*, April, 1940, *34*, 489–498.

The types of polyp of the intestine most frequently seen are adenomas and inflammatory hyperplasia. Polyps are more frequent in males than in females and are most commonly found after forty years of age. They are almost uniformly distributed throughout the large bowel. They frequently precede carcinoma and are an important factor in causing it. If a patient reports bleeding and loose stools a proctoscopic examination should be made. If the lesion is beyond the range of this examination a roentgen examination must be made.

It is hard to demonstrate polyps and other small lesions of the bowel. The contrast technique used by Weber at the Mayo Clinic is valuable but it is long and requires full cooperation of the patient. The authors use a simpler method which is adequate in most cases. A light evening meal is given the day before followed by 2 ounces of castor oil. No food is given after the castor oil but water may be taken. The next morning no breakfast is given. A 2-quart tapwater enema is given with the patient lying on his back and gently rolled from side to side. After the enema is expelled a light barium-buttermilk-water solution is injected slowly. The head of the column is carefully watched to detect any change from a normal convex to a suspicious concave border. The area is then carefully palpated and pressure applied; the area under pressure can be visualized on the fluoroscopic screen. Any small filling defect can be seen clearly. With the area still under pressure a spot-film is taken, as routine films of a barium-filled bowel are not diagnostic.

Seven cases examined by this technique are described and illustrated with roentgenograms. —*Audrey G. Morgan.*

Golden, Ross, and Swenson, Paul C. Experiences with a compression device in examinations of the alimentary tract. *Radiology*, April, 1940, *34*, 457–468.

The writers describe an apparatus used for compression of the stomach or intestine during roentgen examination. It consists of a combined fluoroscopic screen, cassette tunnel and mechanism for switching instantly from a fluoroscopic to a roentgenographic setting. Compression is made by a small cone attached to the screen-holding frame in such a way that it can be moved into the field without delay. Illustrations are given of the apparatus in different stages of its use and roentgenograms are reproduced with the intention of illustrating the method rather than showing the pathologic processes.

This apparatus has been used chiefly in examinations of the stomach and duodenum but it is useful in other regions also. A small field may be delimited and examined with maximum economy of material. Without compression it is useful in examining the esophagus, particularly for varices. Compression films give valuable information in the small intestine, particularly in some cases of ileitis and in intestinal obstruction after the insertion of the Miller-Abbott tube. Compression is not necessary so frequently in the large intestine but the device can be used readily for non-compression exposures in certain positions and for this reason it is used almost as a matter of routine when barium enemas are given.—*Audrey G. Morgan.*

Bell, Joseph C. Some uses of the spot film in the roentgen-ray examination of the gastrointestinal tract. *Radiology*, April, 1940, *34*, 469–480.

The spot film as a supplement to the usual film technique was developed in Europe and it has not been used extensively in this country because of the lack of suitable apparatus readily adaptable to that in use. The author has constructed such apparatus in his own office and used it long enough to know that it is satisfactory. It includes a quick change-over switch for changing rapidly from the fluoroscopic to the roentgenographic setting and for making film exposures, a serial film tunnel with provision for localized compression of the part being examined and a locking device which will automatically keep up any desired degree of pressure. The apparatus and the floor-plan of his gastrointestinal room are illustrated. Serial films of the gastric and duodenal region illustrating the uses of the method are also given. It has proved to be of very great value in demonstrating the niche in duodenal ulcers; it shows them in a much larger percentage of cases than the usual films do. It is an excellent method of demonstrating duodenal diverticula, benign tumors of the duodenum and other lesions in this area and for showing a marginal ulcer in the stoma of a gastrojejunostomy or a jejunal ulcer. It may be used to advantage in demonstrating many lesions of the small intestine and colon. This is particularly true of isolated polyps in the colon and early small carcinomas. Large lesions of the colon are shown better by other methods. Of lesions of the eosphagus only diverticulum and ulcer can be demonstrated to advantage with this type of film.—*Audrey G. Morgan.*

Oppenheimer, Albert. The ileocecal region. *Radiology*, May, 1940, *34*, 545–559.

The author made a roentgen study of the ileocecal region in 86 apparently healthy persons in the Department of Roentgenology of the American University of Beirut. A series of illustrative roentgenograms is given. He wished to study particularly how the food is moved from the ileum into the cecum and from the cecum into the colon.

As a result of his study he concludes that in the terminal ileum, cecum and ascending colon, opaque food is moved on chiefly by systolic tonic contractions alternating with diastolic relaxations. These variations in tonus are fairly rapid in the terminal ileum but very slow in the ascending colon. In the latter the caudad progression of the haustra helps to move the food onward with a sort of dredging process. The food is not moved on appreciably by rhythmic peristalsis. A receptive relaxation of the cecum begins as soon as the food reaches the loops of ileum next to the terminal loop. The cecum is normally low in position when it begins to fill and rises while the contents are moved on into the transverse colon.

The ileocecal valve remains closed while there is rhythmic peristalsis in the terminal ileum; when the food is driven forward by tonic stripping contractions of the terminal ileum it becomes passable. It is not certain whether it acts exclusively as a valve or temporarily as a sphincter. The valve is normally competent for opaque food given by mouth.

The cecocolic sphincter is relaxed while the ascending colon fills but contracts strongly while the contents is being driven into the distal parts by mass peristalsis. This contraction causes physiologic stasis in the cecum.

The appendix is filled by peristalsis of the cecum but is emptied by its own tonic contractions.—*Audrey G. Morgan.*

Erba, Lino. Invaginazione colo-colica acuta nel bambino. (Acute colo-colic invagination in children.) *Radiol. med.*, Aug., 1940, *27*, 623–631.

Invagination of the colon into the colon is quite rare. The author has found only 20 cases in the literature in which roentgen examination was reported. So far as he knows no case of

roentgen demonstration of such an invagination in a child has been reported.

He reports a case in a boy eighteen months of age. For several days the child had had vague abdominal pain and had passed feces mixed with mucus. The evening preceding the examination he had had violent abdominal pain and vomiting. The physician who examined him found a sausage-shaped swelling about 5 cm. long in the left hypochondrium; it was rather hard, with an irregular surface, painful on palpation and slightly movable vertically but not laterally. The physician suspected intestinal invagination and sent the boy for roentgen examination.

A barium enema, given with a low pressure of about 30 cm., rose slowly until it passed the splenic flexure. For a length of 4 cm. in the transverse colon it produced a series of vertical stripes, outlining the wall of the invaginated colon. The head of the invaginated part appeared just to the left of the spinal column. The invaginated part was bounded above by a tortuous opaque line, the ends of which were connected by an arched opaque line, convex distally. Above the invagination there were only traces of barium and the ascending colon and cecum were filled with gas bubbles. The roentgen picture of invagination corresponded to the swelling found on clinical examination.

The pressure was raised gradually and carefully to about 120 cm. and the invagination disappeared. During the several months that have passed since there has been no recurrence.

Objection has been made to the use of roentgen examination in children with acute invagination because of the delay in operation. It is true the time required for barium given by mouth to reach the invaginated part of the intestine would be serious, but the author believes a preliminary examination of the abdomen without contrast should be made with the patient standing, and then a roentgen enema given. This not only makes a rapid diagnosis possible, but in some cases, as in the one described above, further irrigation overcomes the invagination and spares the patient the necessity of operation. There has also been considerable discussion of the amount of pressure permissible; in this case a low pressure during the examination, gradually raised to 120 cm., had only good effects.—*Audrey G. Morgan.*

Pineles, S. Troubles de la motilité et de la sécrétion gastriques chez les enfants. (Troubles in gastric motility and secretions in children.) *J. de radiol. et d'électrol.*, Aug., 1939, *23*, 358–360.

The roentgenographic findings are described in a syndrome that occurs commonly in children of school age. The clinical picture is well known to all practitioners and consists of loss of appetite, epigastric pain, nausea, vomiting, loss of weight and nervousness. Roentgenographically there are noted: (1) retained fluid (hypersecretion); (2) pylorospasm with delayed evacuation; (3) granular mucosal appearance, probably due to excessive mucus. The picture thus simulates that observed in gastritis of adults except that it responds more readily to medical management.—*M. L. Sussman.*

Baensch, W. Zur den Bewegungsvorgängen des Dickdarms bei der "Irritation." (Phenomenon of motility in irritation of the colon.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, June, 1940, *61*, 348–355.

Observations on the motility of the colon are difficult because of the long intervals during which they occur. Motility is controlled by the autonomic nervous system through the plexuses of Auerbach and Meissner. Phenomena of "irritation" do not constitute a disease entity, but are seen in certain psychoneurotic status, in psycholabile individuals, hormonal disturbances (Basedow's disease and acromegaly), and also in all sorts of abdominal conditions (peptic ulcer, urinary calculus, chronic appendicitis, tumor, etc.). The movement of the colon may be divided into two main types: the first serves to dehydrate, consolidate and form the feces while the second is concerned purely with the transport and evacuation of the feces. In a state of irritation the phenomena of the first type are suppressed while those of the second type are accentuated.—*W. A. Evans, Jr.*

Feldman, Maurice. Protrusion of the appendiceal stump following appendectomy. *Radiology*, May, 1940, *34*, 571–572.

Sometimes protrusion of the stump of the appendix into the cecum gives a roentgen picture that resembles that of pathological conditions. In protrusion of the stump the deformity is usually seen in the region of the appendix on the inner aspect of the cecum. It is a nipple-like protrusion with a symmetrical indentation on each side of the nipple defect. Roentgenograms of 2 illustrative cases are given. The pathological conditions from which this picture must be

differentiated are ileitis involving the ileocecal valve, inflammatory changes in the cecum, amebic infection, tuberculosis of the cecum and early carcinoma of the cecum. However there are generally clinical symptoms in these cases that make differentiation possible.—*Audrey G. Morgan.*

Weber, Harry M., and Good, C. Allen, Jr. Invaginated appendiceal stumps roentgenologically simulating polypoid neoplasms. *Radiology*, April, 1940, *34*, 440–443.

The inverted stump of the appendix may persist for some time in the shape of a bulbous mass projecting into the lumen of the cecum. In the roentgenogram it appears as a filling defect in the tip of the cecum at the usual site of the base of the appendix. It may cause intussusception. It cannot be differentiated absolutely from a small polypoid tumor. If the roentgenologist knows that the appendix has been removed and the defect is at or near the medial wall of the cecum it is apt to be the invaginated stump of the appendix.

Four such cases are described and illustrated with roentgenograms. All of the patients had pain and digestive disturbances except one who had no symptoms except stubborn constipation. In each case the small polypoid mass removed on operation proved to be the stump of the appendix.

The best way to demonstrate these stumps is by a modification of the double contrast method of Fischer and Weber. A contrast enema is given and as soon as it is evacuated the colon is redistended with air under screen control. Stereoscopic roentgenograms are then made, using the Potter-Bucky diaphragm with the patient in the best position to show the cecal segment.—*Audrey G. Morgan.*

Ravenel, W. Jervey. Submucous lipoma of the large intestine, with case report. *Radiology*, Feb., 1940, *34*, 217–221.

In 1938 the first case of submucous lipoma of the large intestine ever seen at Roper Hospital in Charleston, South Carolina, was admitted there. The patient, a colored woman of sixty, made an uneventful recovery after the resection of 14 cm. of the transverse colon. The case is reported in detail and the author reviews the literature of the subject. In 1937 Pemberton and McCormack collected 116 cases, and the author reports 5 since that time, making a total of 121 cases published in the English literature to date. The patients may or may not show symptoms. All of the author's 5 cases did—hemorrhage, vague pain in the abdomen, obstruction. The condition is usually diagnosed as carcinoma because of the loss of weight, bleeding, low hemoglobin and the fact that it appears during the cancer age; 72 per cent of these tumors appear during the cancer age. In all of the 5 cases reported by the author there was recovery after resection except in one in which the patient died four days after operation of peritonitis.—*Audrey G. Morgan.*

Stenström, Bo. Über Cholangiographie. (Cholangiography.) *Acta radiol.*, 1940, *21*, 549–570.

It is very important to determine whether any given case of icterus is hepatogenous in origin or caused by obstruction of the bile tract. The author discusses the various clinical and laboratory methods that have heretofore been used for making this differentiation and then describes the more recently introduced method of cholangiography.

This consists of introducing a contrast medium directly into the gallbladder or common or cystic duct, most commonly into the common duct. It may be either primary or secondary. In the former method the injection is made during the operation and in the latter the contrast medium is introduced through the drain of an operation previously performed. For successful results the roentgenologist must have an intimate knowledge of the normal appearance of the bile tract and there must be close collaboration between roentgenologist and surgeon. As it is necessary for the patient to hold his breath it is generally necessary to use local anesthesia, either spinal or splanchnic.

The author has used this method 72 times on 57 patients. Of these cholangiographies 44 were primary, 7 performed under general anesthesia and the rest under spinal anesthesia. The remaining 28 were secondary cholangiographies. They were performed with a strong transportable apparatus, the Siemens' roentgen camera, with 85 to 90 kilowatts, 30 ma., and three to four seconds' exposure time. In the first 47 cases thorotrast was used, but as it is stored in the reticulo-endothelial system and has radioactive properties it is not entirely free of danger and its use was therefore given up. Perabrodil was afterward used in 9 cases and abrodil in 16 cases. A 20 per cent solution of abrodil proved a

good contrast medium; it is water soluble, harmless and comparatively cheap.

The author thinks that with careful technque changes in the common duct can be shown in most cases. The method should be used when it is necessary to show changes in the excretory bile ducts during operation. He gives roentgenograms of a number of his cases, accompanied by brief descriptive notes of the cases.—*Audrey G. Morgan.*

Newell, R. R., and Briggs, Rowland. Cholecystography: optimum voltage. *Radiology*, May, 1940, *34*, 568–570.

The authors tried to improve contrast in cholecystography by using lower voltage, selective filters and by using tetrabromphenolphthalein instead of tetraiodophenolphthalein. Roentgenograms are given showing the results obtained. The tests were done on artificial gallbladders. None of the methods gave any improvement in results. However about 60 per cent of the patients had some unpleasant symptoms after the use of tetraiodophenolphthalein and for that reason it might be worth while making further tests with the tetrabrom. If tetraiodophenolphthalein is used 70 kv. gives as good contrast as 40 kv.—*Audrey G. Morgan.*

Ettinger, Alice. The value of the upright position in gall-bladder examinations. *Radiology*, April, 1940, *34*, 481–488.

Sandström and Åkerlund of Sweden and Bernstein and Eliasz of Germany have recommended examination of the gallbladder in the upright position but it has become a routine method in only a few institutions in this country. The gallbladder should first be focused by fluoroscopic examination in order to get the most favorable angle and favorable degree of compression for the roentgenogram in the upright position. The use of the so-called "snapshot" device, first designed for use in examining the gastrointestinal tract is recommended in this type of examination.

Roentgenograms are given of normal gallbladders and those with various pathological conditions shown in upright examination. The normal gallbladder with the patient in the supine position shows a fairly uniform density. But with the patient standing the fundus is filled with a dense dye while the upper half casts only a faint shadow. This shows that the gallbladder contains biles of different concentrations. Cases illustrating the value of this knowledge are described. Bernstein says that the concentrating function of the gallbladder can actually be observed if films of it are made shortly before intravenous injection of the dye.

In taking films in the upright position gallstone shadows can be projected free of other disturbing shadows. It is often valuable to know whether calcified stones are free or impacted. If the patient is examined first in the prone and then in the upright position the stones will change position if they are free. Occasionally a peculiar shape of the gallbladder is seen in the prone position. In the upright position it is seen to be a bilobed gallbladder, a congenital anomaly not of great importance.

Perhaps the greatest service rendered by examination in the upright position is the demonstration of small transparent stones. In these cases examination in the prone position may show nothing or only indefinite mottling. In the film made in the upright position they collect in the fundus; if they are very close together the gallbladder may appear to be cut off at its lower pole. Sometimes they seem to float in the bile at various levels but this may be due to the artificial conditions of cholecystography. Åkerlund gives a table showing the specific gravities of biles of different concentrations and of various stones which seems to prove that the stones cannot really float. The floating stones are of recent origin and are found increased in size on later examinations.—*Audrey G. Morgan.*

Levene, George, Lowman, Robert M., and Wissing, Egon G. Roentgen diagnosis of the strawberry gall bladder. *Radiology*, April, 1940, *34*, 391–399.

Strawberry gallbladder, also called cholesterosis or lipoidosis of the gallbladder, is one of the earliest forms of disease of the gallbladder. Cholesterol is deposited on the tips of the villi, giving the sectioned gallbladder the appearance of a ripe strawberry. The symptoms are indigestion, gas and distress after meals. Jaundice and colicky pain are not seen. It frequently occurs after pregnancy, which suggests a metabolic or endocrine causation. Among the authors' 30 proved cases 3.3 per cent were in males and 96.7 per cent in females.

Ordinary cholecystography is generally not adequate for diagnosis and a negative result of such a test is not conclusive. After the first cholecystogram has been inspected the authors give

a motor meal consisting of 4 eggyolks and 9 ounces of 40 per cent cream flavored with ginger ale. Within ten minutes the gallbladder contracts. The strawberry gallbladder is much more active than the normal organ. The signs on which they rely for diagnosis are good visibility, active contractions, good compressibility, tenderness over the gallbladder and at the costovertebral angle and rapid emptying. Among 32 cases diagnosed as strawberry gallbladder on the basis of these signs 30 proved on operation to have cholesterosis.

In the discussion Dr. Newcomer referred to Boyd's statement that this condition is always accompanied by a mild degree of chronic inflammation and to the statement of Weiss that the local signs of cholesterosis are those usually associated with chronic cholecystitis. He believes that two of Dr. Levene's diagnositic signs —good visibility and good compressibility—are also characteristic of normal gallbladders. The emptying time of the normal gallbladder varies so widely that he thinks this sign is not reliable. Tenderness over the costodiaphragmatic angle often occurs in duodenal ulcer and kidney lesions. This leaves only local tenderness over the gallbladder.:

Dr. Rhinehart said that nutritional deficiencies seem to have a direct relationship to this disease. Women generally show defective nutrition after pregnancy and nursing.

Dr. Levene said that he believed that strawberry gallbladder is primarily a metabolic disease, probably associated with a glandular disturbance involving the ovaries, liver and possibly the suprarenal cortex and pituitary gland. There must be vitamin deficiencies and calcium disturbances. The changes must be recognized early if diagnosis is to be of any value and the picture he has given is that of early strawberry gallbladder. He does not agree that direct tenderness is the only diagnostic sign. He thinks that good visibility, active contraction and good compressibility of the wall are diagnostic signs, as well as direct and reflex tenderness. Kidney tenderness is lower than the costovertebral angle and while there may be tenderness at that angle from duodenal ulcer that does not destroy its value in the diagnosis of strawberry gallbladder as there are other differential signs between the two diseases.—*Audrey G. Morgan.*

Buisson, Paolo. Obbiezioni ad uno studio sulla colecistografia nel normale. (Criticism of a study of cholecystography in normal individuals.) *Radiol. med.*, Aug., 1940, *27*, 648–652.

The author has always held that the normal gallbladder is opacified and shows a shadow in the roentgenogram with the Graham and Cole intravenous test. If the gallbladder is not visible it indicates some disease of the liver or bile tract. It is generally serious conditions that are shown by this test. Therefore if the test is not reliable a very valuable aid in the diagnosis of diseases of the liver and bile tract must be given up.

Di Giuli published a study of cholecystography in normal individuals in *Radiologia medica*, February, 1940. He reported a study of 38 normal individuals by the cholecystographic test of Graham and Cole. He found that 6 of these supposedly normal individuals did not show any opacification of the gallbladder and therefore concludes that the test is not reliable.

Buisson says that there were very definite sources of error in Di Giuli's examinations. In the first place he allowed the patients to eat a meal the evening before the examination and gave them a cleansing enema between the evening meal and the intravenous injection. This may have accounted for the early emptying of the gallbladder and its consequent invisibility. Also he did not hospitalize the patients but allowed them to go home, merely telling them not to eat. It is quite possible that they did not observe this precaution and that that was the reason for the non-visibility of the gallbladder. Buisson is particularly inclined to believe this because in 2 of the cases a later examination showed opacification of the gallbladder.—*Audrey G. Morgan.*

Tescola, Carlo. Bile calcarea. (Calcareous bile.) *Radiol. med.*, Aug., 1940, *27*, 656–658.

A woman of forty had had dyspeptic symptoms for some years. Ten years ago she had had attacks of pain in the right hypochondrium which had not been repeated since. Nothing was found on physical examination. There was slight pain on pressure below the right costal arch.

Roentgen examination showed nothing abnormal in stomach or duodenum. In the right hypochondriac region there was a pear-shaped body with homogeneous opacity, with small transparent zones here and there. Above it at the width of the body of a vertebra there was another small opaque body the size of a pea connected with the first one by a slightly opaque tract. Apparently the gallbladder was full of

calcareous bile and contained stones. This diagnosis was found to be correct on surgical removal of the gallbladder. It contained a solid block of whitish material that showed all the characteristics of a calcium paste. There were three small cholesterin stones embedded in it. Another small calcium and cholesterin stone occluded the upper end of the cystic duct. The dense contents of the gallbladder were found on chemical examination to be made up chiefly of calcium carbonate.—*Audrey G. Morgan.*

GYNECOLOGY AND OBSTETRICS

Johnston, Albert C., and Sosman, Merrill C. Antepartum roentgenographic diagnosis of fetus papyraceous. *Radiology*, March, 1940, *34*, 261–266.

Fetus papyraceous is a dead, mummified and flattened fetus associated with a living twin. These fetuses can be diagnosed by roentgen examination. The case of one such fetus diagnosed by roentgenograms three months before delivery is reported and illustrated by roentgenograms and the roentgenograms of three other fetuses are given to show the ossification of the skeleton in similar cases. A total of 109 cases have been reported in the literature. Twenty cases were in triplet pregnancies.

The fetus does not lose any appreciable amount of its calcium content and as it usually reaches the age of three to five months before death the centers of ossification are well developed. It is possible to determine the age of the fetus from these centers of ossification.—*Audrey G. Morgan.*

GENITOURINARY SYSTEM

Barbieri, Arrigo. L'indagine radiologica nell'ureterocele. (Roentgen examination in ureterocele.) *Radiol. med.*, Sept., 1940, *27*, 687–700.

Ureterocele is a dilatation of the intramural part of the ureter. It was first recognized on roentgen examination by Lenarduzzi in 1931 and he has given the best description of it yet written. He examined a patient who had pain in the left flank with burning on micturition, pollakiuria and intermittent fever. On descending pyelography it was found that the urinary tract on the right side was normal while on the left the pelvis and ureter were dilated. In the left half of the bladder in continuation with the ureter there was a round opaque spot about the size of a dime with distinct outlines, surrounded by a transparent line about a millimeter in width which separated it from the rest of the opaque urine. This shadow remained unchanged for about two hours; when the examination was repeated in various projections it was found to be intravesical. When the bladder was full the transparent line formed a complete circle, when it was less full it was interrupted at the top and side and was the shape of a horseshoe. The opaque spot represented the cavity of the ureterocele and the transparent line its walls; when the bladder was full it was completely surrounded by opaque urine; when it was not so full the line was interrupted.

The author describes and illustrates with roentgenograms 4 cases in his practice. The first was in a child five months of age and is interesting from the fact that the lesion was in the beginning stage and could not be demonstrated cystoscopically and from the fact that its occurrence in so young a subject supports the theory that ureterocele is congenital in origin. The second case was in a man of twenty-four and was interesting from the fact that it contained calculi and was bilateral, which is very unusual. The third case was in a man of thirty-five and was the largest that has been described. In spite of its size its cavity was free, though in large ureteroceles the cavity is generally filled with detritus, pus or calculi. The fourth case also was in a young patient, a boy two years of age. It showed a U-shaped shadow around the lower end of the ureter. This and Lenarduzzi's sign are the only certain signs of ureterocele, though other signs have been described by other authors.

The question of the comparative value of roentgenography and cystoscopy in diagnosing this condition is discussed. The author's material seems to indicate that the diagnosis can be made somewhat more frequently by cystoscopy than by roentgenography but he does not believe that this is necessarily true. A careful and accurate roentgen examination seems to be of special value in cases in which the lesion is not very well developed anatomically.—*Audrey G. Morgan.*

Lucke, B. Physical factors influencing the growth of cancer (experimental studies based on renal adenocarcinoma in animals). *J. Urol.*, Nov., 1940, *44*, 545–563.

Malignant renal tumors occur in animals as well as man. Animals are susceptible to both an

immature tissue tumor, the embryoma or Wilms' tumor, and a carcinoma, or "hypernephroma." Most investigators now believe the hypernephroma originates from renal epithelium.

It has been found that tumors with a similar structure behave similarly no matter whether found in man or animals. Therefore information can be learned about human tumors from study of animal tumors. The author has found a variety of tumors in cold-blooded vertebrates, in whom they were formerly thought to be rare. In biological investigation cold-blooded animals have certain advantages because of slower vital processes, dependence on environment, less vulnerable tissues and larger cells. The author has especially studied adenocarcinoma of the kidney in the leopard frog, of which over 900 cases have been followed.

The tumors may be solitary or multiple, solid or partially cystic, and vary markedly in size. Metastases are not uncommon. Histologically the tumors resemble adenocarcinoma. All gradations were found from the frankly malignant adenocarcinoma to the benign adenoma.

The author believes that tumor growth should be studied by continued observation of living tissue rather than by histologic study of fixed sections. His method was to transplant small fragments of tumor tissue into the anterior chamber of the eye where their growth can be studied by the microscope. He found that the tumors developed according to definite well defined structural patterns rather than "lawlessly" as is so commonly thought. Unimpeded growths assumed a tubopapillary pattern, but when contact of the growth margin occurred with a firm surface a striking change occurred. Differentiation was lost and invasion of the iris was noted, and the tumor assumed an acinar pattern as had been present in the kidney originally. This shows the effect of environment on tumor growth and that such growth follows a definite pattern.

The author also made a study of growth of renal carcinoma in tissue culture. He found two types of growth, the first in the form of tubules which maintain their tubular form as long as enveloped by the culture medium. When the growth contacts a firm surface, however, the cells give up their tubular form for a membranous form.

Another environmental factor was studied in the response of the growth to temperature. The growth was slower at low temperatures. Vascularization was also less effective and tumor growth less massive at lower temperatures. The effect of temperatures higher than normal was also studied. Here, the initial growth was more rapid but growth retarding factors were effective sooner. Neither high nor low temperatures caused death of tumor cells. Metastases were more widespread at high temperatures. This, the author feels, is due to increased locomotion of the cancer cells.—*R. M. Harvey.*

Barrett, W. A. Primary echinococcosis of the kidney. *J. Urol.*, Oct., 1940, *44*, 389–396.

Echinococcosis is the formation of cysts due to the larva of the dog tape-worm, ***Taenia echinococcus***. The cyst may grow for ten to fifteen years before symptoms develop. The termination is usually fatal unless spontaneous rupture and drainage occur. The human infestation comes from close contact with infected dogs. The ova are ingested orally and liberate embryo in the intestine which invade the intestinal wall and enter the portal system. Hence the predominant site of infection is the liver. In order to reach the kidney the embryo must pass through the hepatic filter and then the capillaries of the lungs to reach the general circulation or through the pulmonary circulation directly from the vena cava without passing through the liver. The incidence of kidney infection is only 2 per cent.

Infestation is believed to occur usually in childhood. Eosinophilia is of help in the diagnosis but the most important test is the intradermal test of Casoni. This is more accurate than the complement fixation test.

Roentgen examination usually shows a large shadow in the kidney area. Dense shadows are reportedly due to the high saline content of the cysts. The pyelogram shows a tumor mass that is not typical in any way. Pelvic deformity and even obliteration occur. Nephrectomy is the treatment of choice in this country in closed localized solitary lesions.

The author reports a case in a woman, aged twenty-three, who complained of left loin pain, frequency, nocturia and hematuria. She had a left upper quadrant mass that appeared to be attached to the kidney. An intravenous urogram showed no function on the left side where a soft tissue tumor could be outlined. The psoas muscle shadow was obliterated. A nephrectomy confirmed the diagnosis.—*R. M. Harvey.*

Kozoll, D. D., and Kirshbaum, J. D. Relationship of benign and malignant hypernephroid tumors of kidney; clinical and pathological study of 77 cases in 12,885 necropsies. *J. Urol.*, Oct., 1940, *44*, 435–449.

The authors divide hypernephroma into two broad classes, a benign and a malignant form. Both types had similar gross features; yellow and vascular, contained a central fibrous core with a cellular cortex, and showed cystic and hemorrhagic tendencies. Histologically both had areas similar to the fascicular zone of the adrenal cortex. The benign form was smaller, well encapsulated, produced no deformity of the kidney, and did not metastasize. It was asymtomatic and found only at postmortem. They call this type "benign hypernephroma," or "hypernephroid adenoma," and the other type "malignant hypernephroma" or "hypernephroid carcinoma." In 12,885 necropsies they found 33 cases of the former and 44 of the latter type. In the 33 benign cases the tumor was entirely an incidental finding at autopsy, having no relation to the cause of death.

The tumors varied from 2 to 4 cm. in diameter. Tumors above 5 cm. were usually malignant. The typical hypernephroid cell is the "foam cell," so-called because of the fat vacuoles present in the cytoplasm surrounding the nucleus. In the benign adenoma these cells were found in solid alveoli, which they filled. Occasionally these cells were arranged in cords or papillae. In the malignant tumors multiplicity of histological types was found much more frequently. Occurring in the same tumor this indicates the evolutionary development of the tumor. Thirty-eight of the 44 malignant tumors showed metastases. They consider a hypernephroma as benign only when metastasis or invasion can be excluded. They feel that the adenoma may be the precursors of the carcinoma. —*R. M. Harvey.*

Fernandez, Mario. Considerazioni su alcune urografie venose. (Study of some venous urograms.) *Radiol. med.*, Sept., 1940, *27*, 711–721.

When intravenous urography was introduced it was thought that it had eliminated the sources of error in the examination of the urinary tract and that it would give all the information that had been obtained formerly by catheterization of the ureters, retrograde pyelography and pyeloscopy. But sources of error have been discovered in this method too. For instance a nervous polyuria accompanied by pyelo-ureteral hyperkinesis may give an absolutely negative pyelogram; a polyuria with stasis in the pelvis from any cause may give a rapid and intense picture of the excretory tract above the obstacle. A good concentration with oliguria gives a clear picture of the kidney but may give an insufficient picture of the pelvis and ureter. Therefore a seriously damaged kidney may not be detected; a hypofunctioning kidney may give a prompt and intense shadow of the pelvis and a hyperfunctioning kidney, as a result of polyuria and hyperkinesis, may fail to give a pyelographic shadow.

The author describes and illustrates with urograms 8 cases in which he carried out intravenous urography and also catheterization of both ureters at the same time, with catheters of the same size introduced to the same height. From a discussion of the results he concludes that it is not possible to depend on intravenous urography alone in examinations of the urinary tract but that this is a valuable method of examination when combined with clinical examination and catheterization of both ureters.—*Audrey G. Morgan.*

SKELETAL SYSTEM

Knutsson, Folke. Die frontale Wirbelkörperspalte. (Frontal fissures in the bodies of the vertebrae.) *Acta radiol.*, 1940, *21*, 597–602.

The author reviews the cases of anterior fissure of the bodies of the vertebrae that have been described before, and describes and illustrates with roentgenograms 3 cases of his own in which there were anterior fissures in the bodies of the lumbar vertebrae. One of the children died from a malformation of the esophagus. In the other two the fissure disappeared when the infants were from two to four months of age. The anterior and posterior centers of ossification fused completely so that a single, completely ossified vertebra was formed. In the third patient there were also anterior fissures in the thoracic vertebrae.

The embryological development of the spinal cord is discussed and the fact brought out that these anterior fissures were due simply to a retardation of development and were not genuine deformities.—*Audrey G. Morgan.*

Pennybacker, Joe. Sciatica and the intervertebral disc. *Lancet*, April 27, 1940, *1*, 771–777.

This is an enthusiastic report of the surgical

handling of 30 consecutive cases of sciatica. Treatment was directed toward elimination of pressure upon the cord or nerve roots in accordance with previous American reports and recommendations. Twenty-eight of the 30 cases were actually found to have changes in the intervertebral disc.

Considerable detail is given as to the anatomy and the pathology concerned with this type of lesion; its clinical picture, the character of the pains, the physical signs and roentgenological evidence. Three possibilities of pressure are cited: that due to herniation of the annulus fibrosus, that due to herniation of the nucleus pulposus and that due to swelling of the ligamentum flavum.

Two cases are discussed to present the clinical picture. It is described as an "ordinary sciatica"—sciatic pain, pain on stretching the sciatic nerve, tenderness of the nerve trunk and diminution or absence of the ankle jerk. Seventeen of the group were males; 13, females. The youngest patient was nineteen; the oldest, fifty-one (most were between twenty-five and forty-five). The duration of symptoms varied from fifteen years to eight weeks. Neither occupation nor habitus seemed to be related; housewives and men engaged in sedentary work seemed just as likely to have the condition. Some type of injury appeared to be associated with all 5 of the cases; half were associated with stooping and lifting—weights as light as a three year old child to that of a 200 pound sack. In a few instances axial injuries appeared to have been associated.

The pain may be sudden in onset or it may be gradual—as a "low back pain" or "lumbago." It may be intermittent or acute and progressive. Flattening and rigidity of the spine were noted in 19 of the cases. When scoliosis was noted, the convexity was to the side of the lesion. Localized tenderness was usually notable (in all but 5, there was tenderness to digital pressure below the sciatic notch). Twenty-five of the cases showed muscular weakness (anterior tibial and calf groups). Paresthesias were noted by 18 of the patients—especially in the calf regions and the outer aspects of the ankles. Two had disturbance of sphincter control with well marked cauda equina syndromes.

The roentgen criteria included: flattening of the lumbar spine and scoliosis; negative fillings at the site of the lesion after injection of 3 to 5 cc. of lipiodol (used in 25 of the cases); absence of filling of the affected root canal. The anteroposterior projection was usually more valuable than either the lateral or oblique studies. The evidence may be more convincing by fluoroscopy than by roentgenographic studies. The author has been removing the lipiodol though he remarks that this might not be necessary (since it is not being done in American clinics and since it results in severe headaches for twenty-four to thirty-six hours following the drainage). It is believed that roentgen studies, including the lipiodol injection, are indicated after eliminating the various orthopedic possibilities.

Having established the diagnosis, treatment should consist of either rest or operation. The rest treatment should mean complete rest for five to six weeks. Operation is advisable for: (1) cases of acute sciatica in whom benefit is not obtained by rest, (2) cases of recurring sciatica, requiring three to four weeks' bed rest yearly and (3) "some cases" of chronic continuous sciatica (those due to herniation of the nucleus pulposus rather than herniation of the disc—the distinction not now being definite). Surgery does not appear to incur hazardous possibilities and recurrences of the pathologic condition are not probable.—*A. A. de Lorimier.*

Bullo, Enzo. Aspetti radiologici e diagnosi differenziale del morbo di Paget della colonna vertebrale. (Roentgen appearance and differential diagnosis of Paget's disease of the spinal column.) *Radiol. med.*, Sept., 1940, *27*, 700–711.

Paget's disease is not extremely rare as Schmorl has reported finding it in 3 per cent of all autopsies and in 4 per cent of autopsies on individuals more than fifty years old. It is a bone disease characterized by progressive increase in the size of the head, enlargement and curvature of the tibias and decrease in height from deformity of the spinal column. The clinical symptomatology consists chiefly of pain at the site of the affected bones, which may radiate to the pelvis and ribs. In some cases pain does not appear until late in the course of the disease.

The bone changes may appear first in the spinal column and not until later in other bones. There is first increased porosity of the bones followed later by increased density, progressing to eburnization. The roentgen picture also varies with the different stages of the disease. Superposition of other tissues, and particularly

the lung outline, may render roentgen examination of the spinal column difficult. Roentgenograms are given showing the appearance of the vertebrae at different stages of the disease. At first they show a slight degree of osteoporosis with disappearance of the fine reticulation of the spongy tissue. Later when the process of new formation of bone has begun the bodies of the vertebrae may present a cottony appearance or the trabeculae may run in longitudinal stripes or they may form a large-meshed network. The form as well as the structure of the vertebrae may be changed. They may be flattened and deformed in various ways and even the intervertebral discs may be affected. They may be flat and may even herniate into the vertebrae. Two vertebrae may even become completely fused.

Differential diagnosis from other bone diseases is sometimes quite difficult; the most difficult differentiation is that from cancer metastases which present extremely varied pictures. The clinical symptoms and bone changes outside the spinal column must be taken into consideration in making the differentiation.—*Audrey G. Morgan.*

Pinelli, Iginio. Curioso reperto di corpo estraneo. (Finding of an unusual foreign body.) *Radiol. med.*, Aug., 1940, *27*, 655–656.

A man was walking along the street carrying a package of high explosive in his left hand. For some reason he dropped it and it exploded, causing injuries of the hand and other parts of the body. He was sent to the hospital and the wounds dressed.

About a month later, after the wounds were healed, he came to the physician and showed a small swelling on the anterior surface of the right wrist with a small recent scar over it. It was small, slightly painful and immovable. It was thought to be a foreign body, probably metal. Roentgen examination showed a foreign body, more transparent than the neighboring bones, lying partly over the epiphysis of the radius, partly in the radio-ulnar space. It was trapezoidal in form with the two surfaces slightly concave inward. In the lateral projection it was almost triangular in form with a smooth posterior margin and an irregular anterior one. Its structure was that of long bone, and it was found to be the first phalanx of a finger. It was removed from the aponeurotic fascia in which it was embedded; there was slight suppuration around it. It was denuded of soft parts. It was hard to understand how this phalanx, denuded of its soft parts, had acquired the force of a projectile, had perforated the skin and become embedded in a region in which there is not much soft and yielding tissue.—*Audrey G. Morgan.*

Vogt, Agvald. Fracture of the column after treatment of psychoses with cardiazol shock. *Acta radiol.*, 1940, *21*, 538–542.

In recent years shock treatment with cardiazol has been commonly used in psychiatric institutions. Fractures of the humerus, femur and other bones have been described but fractures of the spinal column have not been reported until recently. The first case seen by the author in the department of roentgenology of the University Clinic of Oslo was on November 25, 1938. Since then he has seen a total of 48 fractures in 20 patients, 44 of them in the thoracic column.

The intravenous injection of cardiazol after ten to twenty seconds produces violent tonic and clonic fits lasting forty-five to fifty-five seconds. From his observation of these cases the author has no doubt that the strength exercised during these fits is sufficient to break even a normal spinal column. In 7 cases fracture of the thoracic column was demonstrated after one shock. One patient had had 25 shocks before roentgen examination was made. The appearance of the fractures with wedge-shaped narrowing of the vertebrae anteriorly indicates that the fractures occur during extreme forward flexion. The fractures show the same appearance and localization (3d to 9th thoracic vertebrae) as those after tetanus. Apparently, therefore, they occur during the clonic stage of the convulsions.

Roentgen examination should be made before shock treatment in order to avoid confusion with old fractures. If there is bone atrophy shock treatment should not be given. Most of the fractures heal even without treatment or rest in bed. Except in severe cases intensive treatment is not required.

No definite conclusions can be reached with regard to how often fracture of the spinal column occurs in shock treatment.—*Audrey G. Morgan.*

Nordentoft, Jens Munck. Some cases of soldier's fracture. *Acta radiol.*, 1940, *21*, 615–621.

The author describes 4 cases of what he calls

soldier's fracture because it most frequently occurs in soldiers or members of working-battalions, particularly if they have not been accustomed to heavy physical work. It is brought about by continuous, rhythmical, unaccustomed mechanical strain in special locations. Two of the author's cases were in the distal end of the femur, the other two in the tibia. The first symptom is pain without any preceding actual trauma. There is a hard solid thickening of the bone. There may or may not be an actual fracture with separation of the fragments. These cases must not be considered unimportant, however, but the patient must be kept in bed for a considerable time unless he can be given a plaster of paris bandage with which he can walk. If rest is not given veritable fracture will certainly result.

A most interesting point about these fractures is that clinically and roentgenologically they have a marked resemblance to Ewing's sarcoma. In the author's cases roentgen examination showed a periosteal reaction very much like the onion peel deposits in Ewing's sarcoma. Differentiation between the two conditions may be difficult.—*Audrey G. Morgan.*

Beatty, S. R., and Ritchie, Gorton. Osteopetrosis, *Radiology*, March, 1940, *34*, 338–342.

Osteopetrosis or Albers-Schönberg's disease is characterized primarily by increased thickness of the bone with encroachment on the marrow cavity.

A case is described in a child one year of age who had always been under a doctor's care and had had convulsions at intervals; they had increased in frequency for the past two months. His head was large in proportion to his body and he had a definitely mongoloid facies. He was pale, undernourished and small for his age. A convulsion began while he was being examined, he became very cyanotic and before anything could be done to stimulate respiration he died.

Autopsy showed all the bones of the body increased in density. The cortex was thick and the marrow cavities almost completely filled by a network of heavy bone trabeculae. The lymph nodes, spleen and liver showed a compensatory myeloid change. Contrary to statements in the literature there was periosteal involvement in this case.

It is possible that this and similar cases in infancy belong to a different disease with a different pathogenesis from the cases described in adults.

Reports have recently been published of an association of fluorine intoxication and osteopetrosis. It was impossible to determine whether fluorine was an etiologic factor in this case.—*Audrey G. Morgan.*

ROENTGEN AND RADIUM THERAPY

Barnes, R. W. Carcinoma of the prostate; comparative study of the modes of treatment. *J. Urol.*, Aug., 1940, *44*, 169–176.

From a review of the literature it is difficult to draw any conclusions as to the best treatment for carcinoma of the prostate. The author reviews a consecutive series of 677 cases treated in different ways by different urologists which represent the average treatment given by the average urologist. The average age was seventy years. The symptoms in the order of their frequency were frequency, dysuria, slow stream, complete retention, back and hip pain, dribbling, hematuria, constipation and rectal or perineal pain. In non-operated cases the clinical diagnosis was made by a competent urologist. In 398 cases the diagnosis was made clinically and in the remaining 266 microscopically.

Transurethral electrosection of the prostate was used to relieve urinary obstruction in 173 cases, 27 of which had postoperative high voltage therapy. Most of this was supervoltage therapy, from 550 to 900 kv.; four or eight fields were used and 1,200 to 1,500 r was given to each field in series. In the results 155 cases were eliminated from consideration, although alive, because they had been followed for less than two years. There is a slight margin in favor of those receiving irradiation in the two year survivals. In the case of prostatectomy alone and prostatectomy plus irradiation, there is a decided statistical margin in favor of irradiation. However, there were only 8 cases irradiated in this group as compared with 65 prostatectomies alone, so that the figures cannot be given too much weight. There is a slight margin in favor of postoperative irradiation in those resected transurethrally but this is not great.

The author concludes that endoscopic bladder neck resection is the best treatment for obstruction and that postoperative irradiation tends to postpone recurrences. Since cases treated prior to 1937 are not included, later statistics may prove even more favorable.—*R. M. Harvey.*

Günsel, Eberhard. Zur Radiumbehandlung der Induratio penis plastica. (Radium treatment of plastic induration of the penis.) *Strahlentherapie*, 1940, *68*, 694–698.

The author describes 2 cases in which he used radium for the treatment of plastic induration of the penis. One of the patients was aged fifty-two and the other thirty-nine.

As he had only 160 mg. radium-mesothorium available he used an apparatus adapted for irradiation at 3 cm. distance. It consisted of a lead cylinder 1 cm. thick with an inner diameter of 4 cm. The tubes containing a total of 162.34 mg. radium-mesothorium with a filtration of 0.3 mm. silver were placed on a glass disc 2 mm. thick at a distance of 3 cm. from the circular opening with an area 12.6 sq. cm., in such a way as to guarantee a uniform distribution of the irradiation. Below the disc there was a small space in which secondary filters could be placed. It was first used without filtration and then with copper filters 0.1 to 0.5 mm. thick.

In the first case irradiation was given on ten successive days with a total dose of 3,500 r on the dorsal side of the penis where the induration was; in the second case ten irradiations were given in fourteen days with a total dose of 4,000 r. In both cases about three weeks after the end of the irradiation there was a dark red discoloration of the skin and an epidermolysis of moderate degree, which healed in a short time. The induration disappeared so promptly in both cases that it is probable that by increasing the deep action by still further filtration the dose could be decreased and the skin reaction avoided.—*Audrey G. Morgan.*

Pfahler, George E. Roentgen treatment of hyperthyroidism. *Radiology*, Jan., 1940, *34*, 43–52.

The author reports 440 cases treated from 1905–1933 and 61 from 1933 to 1937, making a total of 501 cases, with 445, or 89 per cent, restored to working capacity. This is about the same as the end-results of surgery. Irradiation has the advantage of having no mortality and causing no scars. Moreover, when the fear of operation is removed patients are more apt to come for treatment earlier when there is a greater chance of success. Irradiation does not cause any difficulty in possible later operation. The adhesions sometimes seen also occur in cases that have not been irradiated. The results of irradiation develop more slowly than those of surgery and it has been claimed that this results in damage to the heart but the author thinks more heart injury is caused by the delay due to the patients' fear of operation. Irradiation tends to prevent the development of carcinoma and even to cure it after it has developed. Iodine should not be used in conjunction with roentgen treatment. Irradiation acts particularly on stimulated thyroid cells and if the stimulation is suppressed by iodine the effects of irradiation are not so good.

The author's technique is: 130 kv., 5 ma., 30 cm. distance with the equivalent of 6 mm. aluminum filtration. This is applied through four cervical fields, 5×10 cm., the shape of truncated cones. The rays are directed so that there is cross-fire in the thyroid and thymus region. A dose of 210–280 r is given through each of the fields, generally on the same day, though the fields may be treated on successive days. Not more than eight such series should be given for fear of causing atrophy and telangiectasis. If the patient is not definitely improved after three to five series it is better to try some other method of treatment.

During treatment the patient should rest as much as possible and a high calory and high vitamin diet should be given. Not only does hyperthyroidism cause loss of weight but loss of weight may cause hyperthyroidism. The calories should be supplied chiefly by carbohydrates. Too much protein raises metabolism. The development of hypothyroidism can be prevented by making frequent determinations of metabolism.—*Audrey G. Morgan.*

Overgaard, Kristian, and Okkels, Harald. Über den Einfluss der Wärmebehandlung auf Woods Sarkom. (The effect of heat on Wood's sarcoma.) *Strahlentherapie*, 1940, *68*, 587–619.

The author reviews the previous work on this subject and describes his own experiments on white mice. He concludes that in animal experiment a measured, moderate degree of heat has a specific action in destroying tumor tissue without doing any essential injury to the surrounding normal tissue.

This tumor-destroying action depends on the intensity and duration of the action of the heat. The action of high frequency currents in destroying tumor tissue probably depends on the heat produced and on its intensity and duration, while the frequency used has no special effect. But this does not necessarily mean that

some frequencies may not be more effective than others in the treatment of tumors. The question of optimum frequency, however, is a purely electrotechnical problem concerned with producing the desired effect on the field with the least injury to the surrounding tissue.

The action of heat on tumors may be combined to advantage with roentgen treatment, as these two forms of treatment supplement each other, probably because the two methods affect different elements and influence different vital functions of the tumor cells.

This theory is confirmed by the fact that histological examination of tumor tissue treated with heat shows quite a different picture from that treated with roentgen irradiation; the elements of the cell which are relatively little injured by roentgen irradiation show rapid and intense degeneration on treatment with heat while the elements that are most affected by irradiation are very little damaged by heat.

The question of whether heat treatment of tumors can be used in practice is left open. Previous attempts to treat malignant tumors in man with heat have generally been failures but that was probably due to the fact that it was technically impossible to supply a sufficient amount of heat of measured and controlled intensity to the focus. These technical difficulties have now been overcome, however, and improvement in the results seems possible.—*Audrey G. Morgan.*

Šanda, E. Über die Röntgentherapie der glandulären Tularämie. (The roentgen treatment of glandular tularemia.) *Strahlentherapie*, 1940, *68*, 534–536.

The first cases of tularemia were seen in Hungary in the autumn of 1936; it was supposed to have come from America through Russia. As no specific remedial agent is known the author tried treating the glandular form with irradiation. In the first stage of lymphangitis with fever and exhaustion he saw no effect, though only 2 of his patients came to him in this stage. In the second stage of enlargement of the glands he irradiated the glands with small doses of 100 to 120 r. Retrogression of the gland swelling was not brought about in any case and it was not possible even to prevent increase of the swelling when the irradiation was given in an early stage. But in all the cases the time required for softening and liquefaction of the glands was greatly decreased. This is important for as soon as the glands soften the pain stops and the patient can at least do light work. When the glands liquefy they should be punctured; with irradiation and puncture the course of the disease can be shortened by two or three weeks. Incision should not be performed except in very large soft glands. Incised glands generally require a long time for healing.—*Audrey G. Morgan.*

Clement, R., Gibert, P., and Clenet, E. Roentgenthérapie des adénoïdites de l'enfant. (Roentgen therapy of infantile adenitis.) *Presse méd.*, May 24, 1939, *47*, 786–789.

Roentgen therapy has been found of value in the treatment of hypertrophied and infected lymphoid tissues particularly where surgery is contraindicated. The latter occurs occasionally when the patient is very young or when the type of infection makes surgery dangerous. When there is a tendency to hemorrhage or in the presence of tuberculosis or other infections surgery may also be contraindicated. In at least two-thirds of the cases the results of radiotherapy are excellent, not only for the period immediately following the irradiation but also beyond this time. The therapy is sharply localized to the area desired, the central ray ordinarily being at the mandibular angle or in the auricular region in the presence of an otitis. The technique used was 200 kv. with a 0.5 mm. copper filter. Three fields are treated, each with 360 to 600 r given in three doses at four to five day intervals.—*M. L. Sussman.*

Daniel, G. Roentgenthérapie anti-inflammatoire et anti-infectieuse. (Anti-inflammatory and anti-infectious roentgen therapy.) *J. de radiol. et d'électrol.*, July, 1939, *23*, 289–295.

The author describes his approach to dermatological, oto-rhino-laryngological and gynecological lesions by citing examples.

In treating furuncles, small doses and low voltages are employed. The variations in r delivered with 25, 35, 50 and 100 kv. radiation are explained by quoting absorption figures. For example, with the higher voltages, the unit absorption is less and so a larger dose in roentgens is required for a comparable effect. Variations also occur because of the differences in thickness of the skin in different parts of the body.

If calculated with the ionization chamber, the doses are actually microdoses. However, the

effective dose which depends on the energy absorbed by the tissues is stated to be about 800 times greater. The calculated dose corresponds to those advised by numerous authors. It is extremely low in order to avoid reaction and to allow a uniform rhythm of application.

In acute case of sinusitis, a microdose is applied. If drainage does not occur after this single session, the author feels that surgery is indicated. In the chronic form, larger individual doses are used in series. The type of radiation, hard, soft or medium, depends on the location and depth of the sinus under treatment.

The margin of therapeutic safety is also observed in cases of mastoiditis.

The therapy of chronic gynecological infections varies with the nature of the etiological agent. An effort is made to produce castration in tuberculosis, whereas in the nonspecific forms, this result is diligently avoided. In hyperacute cases with peritonitis, the author is enthusiastic about the excellent effect with low dose radiotherapy as compared to other therapeutic means. In fact, he believes that roentgen therapy is the method of choice in conservative gynecological therapy.—*M. L. Sussman.*

Huguet, J. Posologie de la roentgenthérapie anti-inflammatoire. (Posology of roentgen therapy of inflammations.) *J. de radiol. et d'électrol.*, Feb., 1939, *23*, 49–57.

The author briefly reviews the results obtained in a group of 82 cases consisting of furuncles, carbuncles, paronychias, cellulitis and miscellaneus lesions. Throughout the series a low voltage and low filtration type of radiation was employed. Doses were very small, ranging from 6 r to 25 r as contrasted with the larger dosages advocated by some authors.—*M. L. Sussman.*

Mathey-Cornat, R. Indications de la radiothérapie des affections gynécologiques inflammatoires. (Indications for radiotherapy in gynecological inflammatory affections.) *J. de radiol. et d'électrol*, Sept., 1939, *23*, 390–396.

Anti-inflammatory roentgen therapy occupies a conspicuous place in gynecology for the following reasons: (1) it has a sedative action, (2) it produces a certain amount of resolution of the inflammatory reaction and lengthens the periods of remission, (3) the results are sufficiently beneficial to reduce the frequency of major surgical procedures.

Irradiation is most effective in the chronic form, although certain subacute and recurrent cases may also respond well. Extreme caution is advised in the treatment of acute cases.

The technical factors proposed are: 175 kv., copper filtration, focus-skin distance 40 to 50 cm., feeble r per minute and one of the following methods:

A. Feeble irradiation, 30 to 50 r (10 to 15 r to the ovary).

B. Feeble repeated irradiation to total of 120 to 150 r (40 r to ovary).

C. Unilateral sterilization by fractionation to total dose of 300 r (100 r to ovary).

D. Temporary sterilization by bilateral irradiation, 150 to 200 r to each ovarian field (30 to 70 r to each ovary).—*M. L. Sussman.*

Wintz, H., and Reding, R. La radiothérapie des affections inflammatoires et son mode d'action. (Radiotherapy in inflammatory affections and its mode of action.) *J. de radiol. et d'électrol.*, June, 1939, *23*, 241–247.

The excellent results that may be obtained are acknowledged and the various hypotheses of the mode of action are mentioned. Their study of the clinical manifestations and observance of the humoral manifestations indicates action by shock.

A local direct action is untenable because:

A. Favorable results are obtained by treating distant parts.

B. Roentgen rays have no direct bactericidal action although the bactericidal power of serum increases.

C. Good results are obtained with all sorts of dosages.

D. The humoral symptomatology observed after irradiation is that of shock, as produced by any agent (protein, colloidal substances, etc.) Shock is considered as a result of the abrupt change in colloidal equilibrium of plasma which appears as:

1. Blood reaction: There are variations in pH just as in anaphylaxis in which a short, mild acidosis is followed by an alkaline wave towards the second day. The latter is more or less proportional to the therapeutic effect obtained.

2. Leukopenia: This is usually abrupt and shows a diminution in polymorphonuclear leukocytes. It may occasionally be preceded by an earlier increase.

3. Coagulation time: There is an immediate increase in 80 per cent of the cases. In the remaining 20 per cent, a decrease occurs first.

4. Blood pressure: A fall may or may not be observed.

5. Stability of colloids: A diminution in stability is shown by the Milbradt test (gold number).

6. Hyperglycemia: This has been described in detail by La Barre.

7. Hypervagotonia: Most authors interpret the phenomenon of shock as a vagotonic excitation.

What is the causative agent of the shock?

To explain the immediate phenomena there must be a colloidal disequilibrium which produces a lysis of the leukocytes which in turn sends a protein substance into the blood. Local edema at the point irradiated is explained by tissue inbibition during lysis. The phenonema of shock activate the defense mechanism in which the reticulo-endothelial system plays an important rôle.—*M. L. Sussman.*

Mathey-Cornat, R. Sur la roentgenthérapie anti-inflammatoire et principalement ses résultats cliniques. (Anti-inflammatory roentgen therapy and its clinical results.) *Presse méd.*, April 12, 1939, *47*, 544–547.

The diseases treated can be grouped into (1) skin inflammations; (2) inflammations of the mouth and pharynx; this includes the paranasal sinuses and mastoids; (3) inflammations of male and female genital systems. In the first group the results are usually, but not always, satisfactory. The results are easily interpreted. Technique is simple. Roentgen therapy may be combined with other types of treatment to a varying degree. The second group, which may be called the otolaryngological, may be subdivided into affections of the tonsil and lymphopharyngeal tissue as contrasted with the remaining structures. Hypertrophy of the tonsil responds well to radiotherapy. Skin doses of 600 to 800 r ordinarily produce recession. Sclerotic tonsils are treated with doubtful results. Acute or subacute tonsillitis or peritonsillar abscess can ordinarily be treated with definite results, usually with localization of the inflammatory process or, rarely, resorption. Cures are fairly lasting. The roentgen treatment should be given in two directions: an external transmandibular field and an intrabuccal field, each treatment being 50 to 100 r. Unfavorable results may occur from repeated treatments, a rhythm which is too rapid or individual doses which are too large. Roentgen therapy is also used occasionally as an adjuvant to surgical treatment. In the mouth, roentgen therapy furnishes most constant results. Osteoperiostitis, chronic or subacute phlegmons of the floor of the mouth and submaxillary region as well as lymphadenitis are greatly benefited. Parotitis is particularly responsive. The gynecological inflammations must be divided into the nonspecific and the tuberculous. Roentgen therapy has only been used recently and therefore should be combined with other methods of treatment. Temporary castration occurs for six to twelve months. It can be achieved and limited by careful ovarian irradiation. The various types of therapy are detailed in the article. General tuberculosis must be studied completely and the patient thoroughly examined before proceeding with any form of treatment. The best results of roentgen therapy are obtained in the subactue form, in the absence of intestinal lesions and in the presence of localization to the adnexa.

The author states that the anti-inflammatory action of radiotherapy is based on many factors. Undeniably there is a cellular action exercised on young inflammatory tissue which can be produced with small doses. There is a complex action on connective tissue, vessels and the neurovegetative system.—*M. L. Sussman.*

Ledaux-Lebard, R. La radiothérapie de la maladie de Morton. (Radiation therapy in Morton's metatarsalgia.) *J. de radiol. et d'électrol.*, Feb., 1939, *23*, 71–72.

The disease first described by Morton in 1876 is reviewed in its various aspects: history, etiology, pathogenesis, diagnosis and therapy. The results in 14 cases are presented. Of these, only 9 could be followed a sufficiently long time. Seven of these were said to be completely cured, one considerably improved and the ninth showed no benefit. A moderate penetrating voltage filtered by 5 mm. of aluminum was employed; 200 r was administered to the head of the fourth metatarsal, divided into three or four doses. Most of the cases responded to the first treatments. The second and third series of treatments were necessary in the others.—*M. L. Sussman.*

Corrigan, K. E. Physical factors influencing the difference between 200 and 500 kilovolt irradiation. *Radiology*, Jan., 1930, *34*, 8–12.

It has been shown that great increases in voltage do not result in a very great increase in the numerical depth dose. Therefore if higher voltages have any real superiority over 200 volt radiation there must be some other reason for it.

The author makes an analysis of 200 and 500 kv. radiation with a field 20 × 20 cm. in size and a target-skin distance of 60 cm. The method of measuring forward scatter, back scatter and a number of minor scattering effects which he calls tertiary scatter, are described and diagrams given showing the results of such measurements for the two voltages. Another diagram is given showing the different composition of the 200 and 500 kv. radiation in primary radiation, forward scatter, back scatter and tertiary scatter at a depth of 10 cm. It is probably this difference in composition rather than the difference in the numerical value of the depth dose that constitutes the real difference in these two qualities of radiation. It is probable that the superiority of the 500 kv. radiation is due primarily to the ability of the higher voltage radiation to reach the depth with wave length unchanged in sufficient quantity to be effective.—*Audrey G. Morgan.*

Dresser, Richard, Rude, Joe C. and Cosman, Bernard J. The differences between 200 kilovolt and supervoltage roentgen therapy. *Radiology*, Jan., 1940, *34*, 13–16.

The group engaged in high voltage research at the Massachusetts Institute of Technology has designed and built a supervoltage roentgen therapy unit for use in the treatment of cancer that has been in use for two years. It operates with 1,000,000 volts constant potential, 70 cm. distance, 3 mm. lead plus 7.75 mm. copper filter, 1 to 1.5 ma. and gives an output of 60 to 70 roentgens per minute, air measurement with a thimble chamber of standard design. Surface backscatter is greatly decreased at the higher voltage.

This type of radiation has certain distinct advantages. There is less injury to the skin. The depth dose is larger and the biological effect greater than ionization measurements would indicate. It is not known whether this is due to a real difference in biologic effect or is a result of failure of the thimble ionization chamber to measure the full intensity of the radiation. The depth dose is largely independent of the size of the field. There is less roentgen sickness with the higher voltage treatment, probably due to the fact that there is less lateral scatter and therefore the volume of tissue irradiated is not so great. There is more satisfactory immediate retrogression of deep tumors with high voltage therapy. The authors have seen complete clinical disappearance of carcinomas of the bladder and cervix with a dose to the tumor of 3,000 to 3,500 roentgens in three weeks. But they do not believe that this dose will permanently control such tumors any more than it will a similar type of tumor on the skin. A larger dose will have to be given with the same fractioning or the same dose in a shorter time.

The shorter wave lengths have a more marked effect on the blood. There is no great change in the erythrocyte count but there is a great decrease of leukocytes with a disturbance in the lymphocyte ratio. The return of the white count to normal requires longer than after 200 kv. therapy.

They have so far had no serious injuries but they realize that overdosage of normal structures may cause serious late results. They think that it will take several years of careful observation to determine the safe therapeutic dose of supervoltage roentgen rays.—*Audrey G. Morgan.*

Packard, Charles. The biological measurement of high voltage radiations. *Radiology*, Jan., 1940, *34*, 17–23.

It is generally admitted that doses of supervoltage roentgen rays have not been measured satisfactorily in terms of standard roentgens. Until accurate measurements have been made it is impossible to compare the effectiveness of 200 volt radiation and that of higher voltages. Until accurate physical measurements can be made biological measurements must be used. *Drosophila* eggs furnish an excellent material for making biological measurements. Approximately the same proportion of eggs survives after a given dose whether the radiation is very soft or moderately hard. Using these eggs as material and calibrating the Victoreen dosimeter with the biological results, it was found that for voltages of from 400 to 900 kv. with half-values ranging from 5.0 to 8.0 the biological dose is about 80 per cent of the physical dose.

Further tables are given showing the tissue

doses at 10 cm. depth (field 100 sq. cm., 70 cm. target-skin distance) with different qualities of radiation. The figures show that when the half-value of the beam increases from 5.0 to 8.0, representing an increase of voltage from about 400 to 900 kv., the increase in the dose is slight, being 15 roentgens, or 3 per cent of the skin dose. Therefore high voltage radiation has very little advantage over that at lower voltages, whether judged by the percentage depth dose or the amount of radiation which can actually be delivered at 10 cm. depth.—*Audrey G. Morgan.*

Witwer, E. R., and Leucutia, T. Late sequelae of divergent biologic skin effects produced by roentgen irradiation with varying voltages. *Radiology*, Jan., 1940, *34*, 24–27.

In studying the effect on the skin of irradiation of different voltages usually only the immediate effects are considered. There may be serious late effects, however, which should be taken into consideration. Soft radiation is more apt to cause necrosis than the harder forms. These chronic ulcers may undergo malignant degeneration.

The authors discuss 28 cases of malignant tumors resulting from roentgen irradiation seen at Harper Hospital from 1922 to 1938. Eight of the cases were in roentgenologists, surgeons or dentists who had been subjected to repeated irradiation over a long period of time, with soft rays, 30–80 kv. In the other cases, the treatment had been superficial (50–100 kv., mostly unfiltered) or medium (100–130 kv., 1–5 mm. aluminum). During this same period more than 10,000 cases had been treated in the authors' department with deep therapy (200 kv., 1 mm. copper), or later with supervoltage therapy (600 kv., 7 mm. copper) without a single case of malignant degeneration, though in about 10 per cent of the cases atrophy and even telangiectasis had resulted from the treatment.

This would indicate that deep roentgen therapy causes less damage to the skin than the superficial form and that supervoltage therapy is least dangerous. In treating skin conditions the upper limit of the voltage range should be used and some filtration if possible. Medium therapy can be replaced in some conditions such as tuberculous lymphadenitis, toxic goiter, benign gynecologic hemorrhage, etc., by deep therapy, and supervoltage therapy is of decided advantage over deep therapy in protecting the skin and normal tissues in cases in which large deep doses and long-continued irradiation are necessary.—*Audrey G. Morgan.*

Costolow, William E. Clinical aspects of supervoltage roentgen therapy in cancer. *Radiology*, Jan., 1940, *34*, 28–33.

The author describes and illustrates the supervoltage apparatus that he has been using since 1933. As voltage increased from 130 to 200 kv. there was a marked increase in the number of five year cures. It was hoped that similar improvement would be seen when voltage was increased to 500 kv. But it is very hard to compare the results obtained in previous years with 200 kv. and those obtained now with 500 kv., as so many other factors besides the voltage have been changed. Tables are given showing the author's results in carcinoma of the cheek, of the esophagus, the bladder, the prostate and the cervix. As the carcinomas of the cheek were near the surface, adequate dosage could probably have been given with lower voltage. The supervoltage results in carcinoma of the esophagus have not been any better than those of ordinary high voltage therapy. The results in cancer of the bladder have not been particularly encouraging though there has been some degree of palliation and he believes that in cancer of the prostate the regression of the tumors under supervoltage treatment was greater than with the 200 kv. technique.

He has treated 178 patients with cancer of the cervix with high voltage roentgen rays and radium. The number of patients treated four and five years ago is too small to give any particularly valuable information. Palliation and primary retrogression have been improved since the introduction of supervoltage therapy and pelvic gland pathology has been overcome in a greater percentage of cases.—*Audrey G. Morgan.*

Schmitz, Henry. The reaction of carcinomas of the cervix to known doses of 800 kv. roentgen rays; the five, four and three year survival rates. *Radiology*, Jan., 1940, *34*, 34–37.

The author discusses the results of treatment of carcinoma of the cervix with 800 kv. radiation. In 1933, 17 cases were treated, in 1934, 27 cases and in 1935, 28 cases. The five year survival rate for the first group was 52.93 per cent, the four year survival for the second group 56.67 per cent and the three year survival

for the third 67.56 per cent. These survival rates are better than those obtained with 200 kv. radiation and radium.

Detailed histological reports of 14 cases are given. In 4 of these cases, or 30 per cent, the carcinoma had absolutely disappeared after treatment; in 3, or 20 per cent, degenerated tumor cells were found, and in 7 cases (50 per cent) there was recurrence after a primary disappearance of the tumor.—*Audrey G. Morgan.*

Discussion of symposium on the differences between 200 kilovolt and supervoltage roentgen therapy. *Radiology*, Jan., 1940, *34*, 37–42.

This is a discussion of a number of papers on the above subject read before the twenty-fourth Annual Meeting of the Radiological Society of North America and published in *Radiology* for January, 1940. (See above abstracts.)

Dr. Glasser emphasized the importance of accurate comparisons of 200 kv. and supervoltage therapy and asked Dr. Packard the reason for using a sheet of celluloid almost 1 mm. thick on his *Drosophila* eggs. Dr. Packard replied that equilibrium between the secondary beta radiation and the primary beam was brought about by the layer 0.8 mm. thick which he used.

Dr. Henshaw discussed Dr. Packard's findings with *Drosophila* eggs and said that the interest of clinical roentgenologists in them showed that there had been no satisfactory answer to the question of the dependence of radiobiological reactions on wave length. Dr. Packard's work is interesting but only shows that the *Drosophila* eggs and the ionization chamber do not give the same measurements for all types of irradiation.

Dr. Taylor defended the accuracy of the thimble ionization chamber and said that a reason must be found for the difference between its measurements and those obtained by biological methods.

Dr. Garland said that the arguments in regard to the superiority of supervoltage radiation somewhat resembled a comparison of the results of surgery with a 2-inch or an 8-inch knife. The results depend on the skill of the operator, not on the length of the knife or the voltage of the machine. Dr. Witwer's paper on late reactions from low voltage radiation was not conclusive. Bad effects would also result from high voltage radiation if unskillfully used. Bad late results have been seen from radium which is equivalent to about 2,000 volt roentgen irradiation.

Dr. Ward suggested frequent examination of the vault of the vagina as a method of checking the depth dose. If this is done carefully it will show that higher voltage gives a definite increase in dosage.

Dr. Allen suggested that the malignancy resulting from irradiation reported in the paper of Dr. Leucutia and Dr. Witwer was perhaps not due to the low voltage in itself but that it was rather the result of repeated treatment over a period of years. He has treated many similar cases with no post-irradiation malignancy.

Dr. Laurence said that theoretically about 100 per cent more skin tolerance would be expected at 1,000 kv. than at 200 kv. This is based on a paper published by Dr. Lauritsen some years ago. His curve, however, was not very accurate and Dr. Laurence has worked out curves by somewhat different methods that show a difference of only 5 to 25 per cent instead of 100 per cent. He thinks an attempt should not be made to compare theoretical and clinical results until more accurate methods of measuring the dose of supervoltage radiation are established. The curves mentioned above were based on free air measurement of the dose. If measurements of the dose at the skin surface, including backscatter, are used there is practically no difference in the reaction at 200 kv. and that at 1,000 kv. This is shown in a curve published by Mayneord about a year ago.

Dr. Corrigan said that he used a reasonably accurate open air chamber and that he had been able to check the ordinary thimble chamber against it up to about 550 kv. with no significant divergence.

Dr. Schmitz said that supervoltage should be used only in large deep tumors. At present there is only empirical evidence of its superiority. Final proof has not yet been brought by the biologist, the physicist or clinician. Not enough cases have been reported to prove its final superiority. The necessity for supervoltage cannot be proved until a large number of five year survivals have been reported.

Dr. Packard, in closing, said that the difference between the biological and Victoreen measurements had not yet been explained satisfactorily and that that was one of the questions that would have to be answered in the future.—*Audrey G. Morgan.*

MISCELLANEOUS

Piergrossi, Aldo. Metodi ed applicazioni della teleroentgenterapia. (Methods and applications of teleroentgen therapy.) *Arch. di radiol.*, Jan.–Feb., 1940, *16*, 67–86.

The greater power attained by roentgen apparatus has made it possible for many years to increase the distance from the focus to the skin. For this reason Coutard was able to devise his method of protracted irradiation with fractional doses with focal distances of 80 cm. to 1 meter. The results obtained with this method stimulated Palmieri to use still greater focal distances of from 1 to 7 meters. This is the method of teleroentgen therapy, which consists of irradiating with very long focal distances. This brings about greater homogeneity of irradiation both on the surface and in the deep tissues.

There are two methods of teleroentgen therapy. The first is the method of Palmieri or local teleroentgen therapy in which a circumscribed part of the patient's body is irradiated at a distance of 7 to 8 meters. The second is total teleroentgen therapy in which the patient's whole body is irradiated.

The advantage of the Palmieri method is to bring about a roentgen irradiation which has practically the effect of radium therapy. The focus of irradiation is brought, so to speak, into the deep tissues and by continuous or subcontinuous irradiation for days, large doses of hard rays can be given with weak local intensity. Total irradiation gives a very homogeneous irradiation of the whole body, obtaining special biological effects with small doses of radiation.

The laws on which the increase of the deep dose is based are discussed and the radiobiology of the two methods reported. The Palmieri method is used chiefly in localized tumors, such as those of the uterus and of the skin, and others which are very radioresistant, such as cancers of the mouth, the upper respiratory tract, the stomach and the lungs. The results in such cases have been very good. Total teleroentgen therapy is used primarily in diseases of the blood-forming organs, particularly in leukemia and lymphogranulomatosis. It is also used in generalized neoplasms and in certain generalized dermatoses.

In both of these methods of teleroentgen therapy the blood picture must be closely watched as there is a possibility of injuring the blood cells. This is particularly true of the total form.—*Audrey G. Morgan.*

Bignami, Carlo. Reazioni ed alterazioni locali e generali da roentgenterapia a 350 kV. (Reactions and local and general changes in roentgen therapy using 350 kilovolts.) *Radiol. med.*, April, 1940, *27*, 271–283.

Among the many techniques designed to produce the greatest effect on deep-seated lesions without injuring the skin or producing injurious local or general changes, the most recent and the most common is the use of very high tensions (300 to 1,000 kv.). The author has experimented with the use of 350 kv. irradiation and noted the differences as compared with that at 170 kv.

He studied 57 patients with cancer of the portio of the uterus who had been treated first with radium inside the uterus and then with roentgen therapy of the pelvis with the following technique: 350 kv., 4 ma., filter 1 mm. copper and 1 mm aluminum, half-value layer 4.32 mm. copper, focus-skin distance 30 cm., radiation 9 r per minute, fields 320 sq. cm. The patients were forty to sixty years of age and in good general condition. The pelvis was irradiated through two fields (hypogastric and sacral) over each of which 3,000 r was given at the rate of 150 r a day; total dose 6,000 r.

This treatment as compared with treatment at 170 kv. showed: (1) less injury of the skin; (2) at least as good results with reference to visceral disturbances and roentgen sickness; (3) a little more injurious action so far as weight and blood pressure were concerned.

On the basis of the effects obtained on the blood in previous experiments as compared with irradiation at 170 kv. that is to say less lengthening of coagulation time, less marked decrease of cell resistance and changes in the blood count similar to those of 170 kv. therapy or even less serious, he concludes that the use of high tension therapy is preferable to that with lower tensions in many diseases, particularly when the pathological focus is deep-seated and requires large dosage.—*Audrey G. Morgan.*

Fournie and Frezouls. La radiophotographie. (Roentgen photography.) *J. de radiol. et d'électrol.*, Aug., 1939, *23*, 353–355.

The method of de Abreu of Brazil was followed in the examination of large groups of men in the military service. It was found that the former examination by simple roentgenoscopy was inadequate and inferior for several reasons, but mainly because of the lack of a permanent

record. Ordinary roentgenography is too expensive a procedure for such large groups. It is concluded that roentgen photography is an effective, practical, rapid and economical method of survey, particularly for uncovering tuberculous lesions.—*M. L. Sussman.*

Dariaux, A., and Desgrez, H. La localisation des corps étrangers par la méthode de Strohl. (Localization of foreign bodies by Strohl's method.) *Presse méd.*, Sept. 20, 1939, *47*, 1349–1350.

The principle of this method involves the use of two metallic reference points *M* and *N* placed on a surface perpendicular to the normal ray and symmetrical to it. The distance *M N* is equal to half the perpendicular distance from the cathode *C* to the line joining *M* and *N*. Lines parallel to the triangle *M* and *N* establish a similar triangle. The base will be contained twice in the corresponding height. Assuming a foreign body *P* within a patient part, the tube is moved until the shadows of the foreign body correspond successively to those of the reference points. Marks are made on the fluoroscopic screen accordingly at P_m and P_n. Since triangle P_mP_nP is similar to triangle *MNC*, the distance P_n will be equal to half the distance between the foreign body and the screen. The deeper the foreign body the smaller the error. One of the most important features of the method is the fact that the patient does not have to be moved in order to make the examination.—*M. L. Sussman.*

Sugiura, Kanematsu. The biological measurement of gamma rays in "equivalent roentgens" with mouse sarcoma 180 as the test object. *Am. J. Cancer*, Nov., 1939, *37*, 445–452.

The purpose of this study was to evaluate the effectiveness of 200 kv. roentgen therapy with that of gamma rays. This comparison was made on the basis of relative lethal dosages of either for tumor cells (mouse sarcoma 180).

The irradiation was given at 200 kv., 30 ma. using 0.5 mm. copper plus 1.6 mm. aluminum filters, and a distance of 50 cm. (the intensity being 59 r per minute). Tumor fragments were exposed to dosages of 500 r and increments of such up to 3,000 r. With 500 r, no effects were noted; with 1,000 to 1,500 r inhibition of growth amounted to 7 and 28 per cent respectively. With 2,000 r, there was a 62 per cent inhibition, while with 3,000 r complete inhibition resulted.

The radium studies were conducted with radon bulbs; 843, 665, 575 and 712 millicuries, respectively. The filter values were 0.5 mm. platinum. Adding half the thickness of the tumor fragments, the distance from the effective point source to the center of the tumor was 10 mm. Dosages administered were 5,000 and increments of such up to 30,000 millicurie-minutes. Transplantability was not inhibited by irradiation of 5,000 or 10,000 mc-min. With 15,000 mc-min. there was a 20 per cent inhibition; with 20,000 and 25,000 mc-min., 60 and 85 per cent, respectively, while at 30,000 mc-min. viability was completely destroyed.

On the basis of these studies, the author concludes that for mouse sarcoma 180, the equivalent values of 200 kv. roentgen radiation as compared with gamma radiation at 1 cm. distance is 96 to 114 r/min./gm. This compares with the Failla and Marinelli figure of 111 r/min./gm., based on physical measurements and the Henshaw and Francis figure of 93.2 r/min./gm. or the Muller figure of 103 r/min./gm., both figures based on the studies of the *Drosophila* pupae.—*A. A. de Lorimier.*

Ralston, H. J. The immediate and delayed action of x-rays upon the protozoan *Dunaliella salina*. *Am. J. Cancer*, Oct., 1939, *37*, 288–297.

The effects of roentgen radiation may be delayed. Wyckoff and Luget showed that after irradiating yeast cells there rapidly followed the development of two-celled colonies—but these die without further budding. Other observers have noted similar inhibition of the reproductive function of living cells after being subjected to roentgen radiation.

The author has studied changes in motility and growth rates of colonies of protozoa so treated. The kilovoltage used was 52; the effective wave length (unfiltered) was 0.33 Ångströms; the intensity, 54.4 r per minute. After applying seven to eight hours of such exposure, death was produced in 100 per cent of the organisms, immediately or within sixteen days. With shorter treatment, giant and odd shaped forms appeared after a few days. The percentage of such variants increased with exposure time.

The author concludes that two separate processes are involved, one affecting the cytoplasm of the cell and causing death; the other

acting indirectly by way of the nucleus inhibiting reproduction.—*A. A. de Lorimier.*

Goldfeder, Anna. Respiratory changes in vitro in normal and malignant tissues following irradiation. *Am. J. Cancer*, August, 1939, *36*, 603–608.

By tissue culture experiments, the author has demonstrated an inhibition of growth with a dose of 25,000 to 30,000 r (single treatment) to various types of tissue: kidneys of very young rats or mice, mouse sarcoma 180, human myxosarcoma and embryonic chick heart. These dosages did not inhibit the respiratory quotients of the tissues. However, there was a marked decrease in oxygen consumption as well as in aerobic and anaerobic glycolysis. These decreases were greater for sarcoma 180 than for normal kidney cells.

The author concludes that the respiratory processes of mammalian tissues were much less vulnerable to a given dose of radiation than the proliferative processes. The effective dose of radiation depends upon the type of rays; for instance, 30,000 r or a dosage of 4,164 mg-hr. of gamma rays produces no apparent effect upon respiration, whereas a dose of 3,931 mc. radon (beta particles plus gamma radiation) did produce a decrease in respiration.

Since these dosages all exceed tolerance dosages for the animal itself, it is assumed that the action of radiation is not direct but rather that it is an indirect one exerted through the blood and lymph channels.—*A. A. de Lorimier.*

Grand, C. G. Neoplasm studies. VI. Granulocytic accumulation following in vivo roentgen irradiation of mouse sarcoma 180. *Am. J. Cancer*, August, 1939, *36*, 540–550.

Goldfeder reported that tissue cultures of sarcoma 180 were not killed with roentgen-ray dosages as great as 20,000 r. Daels observed an invasion of eosinophilic granulocytes into a uterine epithelioma which was previously exposed to irradiation. Schwarz has stated that roentgen treatment is more effective when hyperemia or inflammation is induced concurrently with roentgen irradiation.

The activity of granulocytes can be studied by observing tissue implants. In general, injured tissues have been found to attract granulocytes. Irradiated implants do likewise—apparently indicating that a chemotactic agent has been liberated. Transplantability of such tumor tissue is diminished the longer it may remain in the host following roentgen irradiation. With increase in granulocytes, necrosis of the tumor occurs. There follows absorption of the necrosed tumor while lymphocytes, histiocytes and fibrocytes appear and persist until absorption is complete. The granulocytes themselves begin to appear at about six to twelve hours after irradiation, increasing in numbers until forty-eight to eighty hours, thereafter showing less and less motility. After complete necrosis of the tumor, the granulocytes become scanty or disappear entirely. The less the roentgen irradiation, the less is the granulocytic reaction. —*A. A. de Lorimier.*

Clemmesen, Johannes. The influence of roentgen radiation on immunity to Shope fibroma virus. *Am. J. Cancer*, March, 1939, *35*, 378–385.

Various observers have noted that after roentgen irradiation, animals suffer a decreased resistance against bacterial invasion. Chrom has ascribed this effect to an influence upon the reticulo-endothelial system. Others have noted a similar decrease in resistance to inoculation of tumor or leukosis after roentgen irradiation.

This report concerns a study of irradiated rabbits inoculated with the Shope fibroma virus. When this virus is inoculated intradermally into control or normal animals, tumors develop but they regress after about two weeks —leaving an immunity whis is resistive against subsequent inoculations. With intramuscular injections, the tumors are likely to grow to large dimensions. Intravenous inoculations are quickly resisted.

The irradiated group received 300 to 700 r of a quality as produced with 200 kv. (peak) and a filter of 1 mm. Cu plus 0.5 mm. Al (half-value layer 1.48 mm. Cu), the distance being 80 cm.

After intradermal inoculation of the virus, tumor growths attained greater dimensions and a longer growth period among the irradiated group. Likewise, with intramuscular inoculations, the growths attained larger dimensions in the irradiated groups. After attaining immunity, roentgen irradiation did not appear to reduce the resistance to the virus.

The authors conclude that roentgen irradiation is comparable in effect to that of tar or trypan blue—all reducing the natural resistance against inoculations of the Shope fibroma virus.

It is suggested that these effects are concerned with the reticulo-endothelial system.—*A. A. de Lorimier.*

Henshaw, P. S., and Francis, D. S. Further studies with seedlings on the question of wave length dependence of radiobiological reactions. *Am. J. Cancer*, March, 1939, *35*, 386–400.

Numerous investigations have been conducted to ascertain whether there is a wave length dependence among radiobiological reactions with high energy radiation (therapeutic roentgen rays and gamma rays).

As tests objects, the authors have been using *Lycopersicum* and *Triticum* seedlings. Previous studies had indicated a greater sensitivity of the *Lycopersicum* seedlings to gamma rays as compared with 200 kv. roentgen rays.

The 200 kv. radiation was given with a filter of 3.22 mm. Cu plus 2.44 mm. celluloid; a focal-filter distance of 34 cm. and a focal-test material distance of 40 cm. The intensity was 19 r/min.

The irradiation with 700 kv. was given with filters of 1 mm. lead plus 3 mm. Cu; the focal-filter distance being 61 cm. and the focal-test material distance being 69.9 cm. Again, the intensity was in the neighborhood of 19 r/min.

The effects of the irradiation were determined four days after treatment. Results were based on linear growths of the primary roots of the two seedlings. Preliminary studies indicated that for 700 kv. therapy, the growth rates were greater than when 200 kv. therapy was applied in the case of *Triticum*, whereas the reverse held true for *Lycopersicum*—indicating a differential response. It was thought that the filtering effect of the secondary filter, the secondary radiation off the celluloid might be a factor. Therefore a 3 mm. thickness of celluloid was placed both in front and behind the test materials. It was then found that at 200 kv. the results were practically the same as before whereas at 700 kv. *Lycopersicum* showed considerably less change in growth.

The authors conclude that these studies support previous evidence as to wave length dependence and they believe that the biological effect will be found to run a parallel with ionization. Therefore they emphasize the importance of devising a means to measure the ionization at the point where the biological change is to be produced.—*A. A. de Lorimier.*

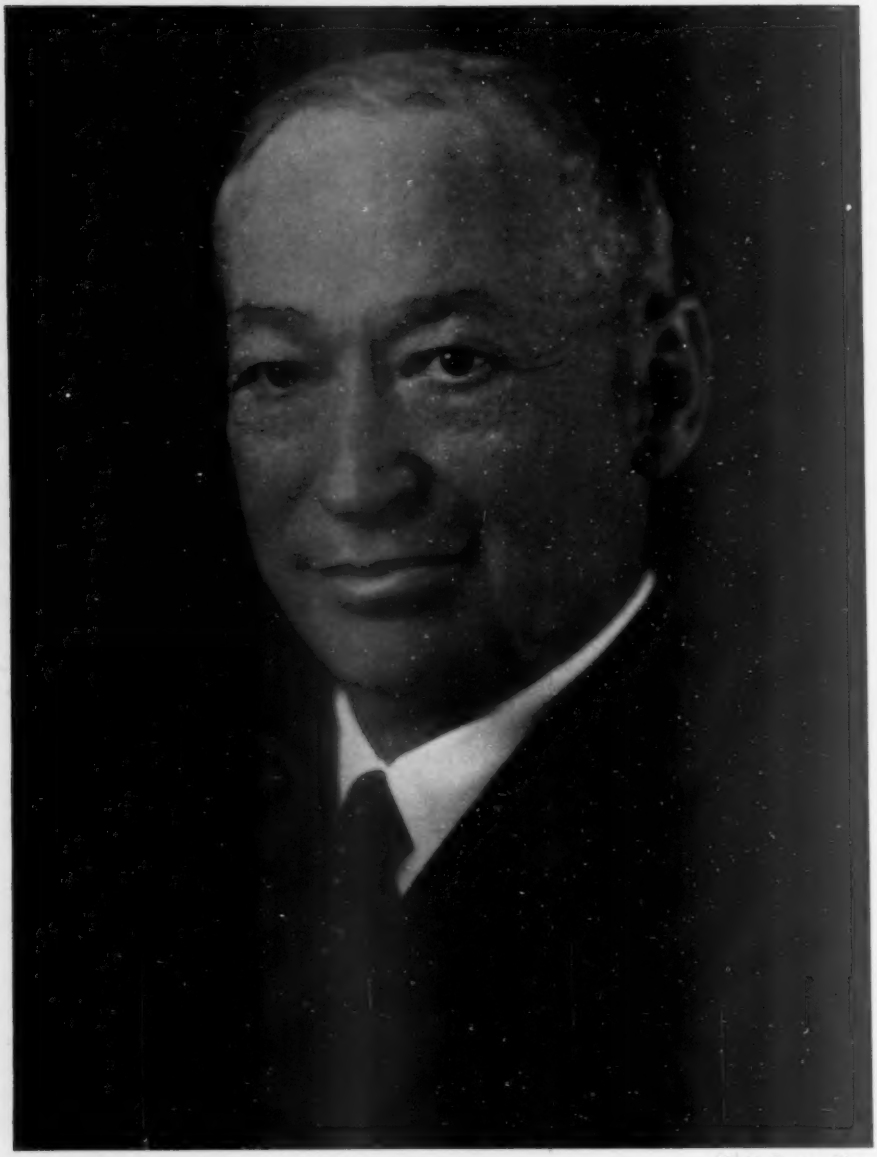
van Everdingen, W. A. G., and Noyons, A. K. M. The irreducible metabolism and specific action of ultra short waves. *Acta radiol.*, 1940, *21*, 39–52.

The question of the specific action of ultrashort waves has been discussed ever since these waves came into use. Investigation has been limited to discussion of the manner in which the energy is absorbed by the tissue. Nothing is known as yet of the action of the absorbed energy in the tissue itself.

A certain amount of heat is always produced in the absorption of high frequency currents by living tissue. The author in his investigations used the method of trying to determine whether there is any action of the waves on irreducible metabolism that is not explained by the heat effect. By irreducible metabolism he means the lowest value of the metabolism of the animal without movement and under ordinary room conditions.

To determine this he measured the irreducible metabolism of different living tissues before and after irradiation and also during the whole period of irradiation. The rather complicated apparatus by means of which he generated and transmitted the waves 16 cm. in length and measured the irreducible metabolism is described in detail and illustrated.

On irradiating tissue pulp of the gastrocnemius muscle of the frog he found that there was no change in the irreducible metabolism when the heat effect was eliminated. On irradiating the larvae of the meal worm (*Tenebrio moliter*) he found a great increase of irreducible metabolism without heat effect. There was a similar but slighter action on earth worms. On irradiating fertilized hens' eggs he found there were two periods, one from the first to the eleventh day and the other from then to the twentieth day, during which the effects of short wave irradiation were almost diametrically opposite. Probably the very injurious results of the irradiation during the first six days were due to the absorption of radiant energy either by the embryo or by other parts of the egg which possibly changes the physicochemical structure in some way. Further study is necessary to clear up this problem. Debye's dipole theory will probably prove of value in explaining the specific action of ultrashort waves on living tissue. —*Audrey G. Morgan.*



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WILLIAM M. DOUGHTY

President of the American Roentgen Ray Society

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